Pediatrics

VOLUME 2 JULY, 1948 NUMBER 1

ORIGINAL ARTICLES

TREATMENT OF INFANTILE DIARRHEA WITH STREPTOMYCIN AND AN ORAL AMIGEN MIXTURE

By ELVIRA GOETTSCH, M.D., GEORGE COBLEY, M.D., AND MARY MULLOY, M.D.
Los Angeles, Calif.

PERSISTENT search during the last half century for the infectious agents responsible for infantile diarrhea resulted in controversial shifts of opinion in regard to the primary etiologic significance of organisms of the colon group and the viruses. During the second decade of the twentieth century Moro[1] grew colon bacilli from the duodenum of infants with diarrhea and suggested that these organisms were of etiologic importance. Many investigators, Plantenga[2-5] and others, elaborated and confirmed the findings. Marriott [6, 7] and his followers pointed out the high incidence of mastoiditis associated with severe parenteral diarrhea, and stressed the predominance of bacteriologic cultures of the colon group from the mastoid and, at times, from the circulating blood of infants afflicted with diarrhea. Hartmann[8] reported on bacteriologic cultures in 13 infants with diarrhea and mastoiditis; in five patients at operation, cultures from the mastoids grew out colon bacilli of the communior type; in one infant Str. viridans was recovered; in another Ps. aeruginosa was isolated; and in the remaining six infants the mastoid cultures were sterile. Dick, Dick and Williams[9] investigated a severe epidemic of diarrhea in a foundling institution and recovered colon bacilli from the blood and mastoid cultures in many of the infants; they presented evidence that the infection was caused by ingestion of unsterile feedings of powdered milk contaminated with living organisms. Recently, Ensign and Hunter[10] described a milk borne epidemic of diarrhea in newborn infants attributed to milk contaminated with the organism Ps. aeruginosa; the bacterial contamination gained entrance through a rag which dripped into the pasteurized milk of one dairy.

During the last decade interest has centered on the etiologic importance of viruses in diarrhea, particularly in newborn infants. Lyon and Folsom[11] described three epidemics

From the Department of Pediatrics, University of Southern California School of Medicine and the Children's Hospital, Los Angeles, California.

Read by title in part at the Annual Meeting of the Society for Pediatric Research, Stockbridge, Mass., May 1947 and presented in full at the Areal Meeting of the American Academy of Pediatrics, Salt Lake City, Utah, September 1947.

(Received for publication March 27, 1948.)

in their community in which influenza was prevalent; they suggested that diarrhea of the newborn was an expression of the effect of this virus in the small infant. Light and Hodes[12] isolated a filterable virus from the stools of infants with diarrhea, which on intranasal injection into calves produced bloody mucoid diarrhea in the animals. Buddingh and Dodd[13] produced lesions on the scarified cornea of rabbits with an inoculum of stool from infants during an epidemic of diarrhea. For further details the reader is referred to the excellent reviews of epidemic diarrhea of the newborn presented by Abramson and Frant[14-18] and by Dodd.[19]

Since no specific therapy for either the gram-negative organisms of the colon and influenza groups, or for viruses existed, treatment was directed in the last 20 years to correction of the electrolyte disturbances brought on by dehydration, acidosis, and renal dysfunction. With more complete understanding of the electrolyte deficiencies provided by the classic studies of Gamble,[20-28] Marriott,[29-30] Butler,[31-35] Guest,[36-40] Darrow,[41-44] Hartmann,[45-52] and others, more perfect replacement therapy has resulted in progressive reduction of mortality. However, in spite of modern sterilization of formulae, careful nursery isolation, and improved intravenous technics which permit continuous infusions, the mortality remains alarmingly high, especially in epidemics of fulminating cases of the disease and particularly, in very young infants. Dodd et al[53] have recently reviewed the mortality statistics from various regions in the world since 1922.

Epidemic Observed in 1945

In March of 1945 a severe epidemic of diarrhea developed on the infants' ward of the Children's Hospital in Los Angeles. A survey of 101 infants involved in the epidemic showed that 41 infants had diarrhea; four patients were admitted with the disease and 37 contracted it on the ward. Fifteen infants were critically ill, 12 were acutely ill and 14 were moderately ill.

The general plan of therapy in the critically ill infants was replacement of electrolyte loss by constant intravenous infusion with physiologic saline, sixth molar sodium lactate solution, and parenteral amigen solution (2.5% amigen, 2.5% glucose, and 0.45% saline). Transfusions of plasma and blood were given when indicated. Sulfa chemotherapy and penicillin were used to combat infection. In the moderately ill patients hydration was maintained with clyses of 5% glucose in saline or with amigen solution in the concentration stated above. Early in the course of the diarrhea all of the infants received a special oral amigen mixture devised to simulate the mineral, protein, and carbohydrate content of skim milk.

The morbidity was 40%; the uncorrected mortality was 20% and the corrected death rate was 7%. Of 36 infants admitted for surgery and free of infection on entry 16 (44%) contracted diarrhea post-operatively. Five infants were critically ill and three succumbed; these deaths were not attributed to diarrhea because the underlying surgical condition was judged to be incompatible with life. Of 65 medical patients, 25 (38%) had diarrhea; 21 infants contracted the diarrhea on the ward. Of ten infants with severe diarrhea, five died; in three of these infants death was attributed to diarrhea, in the other two babies the underlying condition was not considered compatible with survival.

We were impressed with the frequency with which bacteriologic cultures of Esch. coli were obtained from the nasopharynx, the ears, and the catheterized urine of infants with protracted diarrhea.

Case Reports

Protocols in detail of two patients who contracted diarrhea on the ward in the epidemic of 1945 follow:

Case 1: D.S. (45-836) Death resulted from diarrhea contracted on the ward.

A seven-week-old male infant was admitted with severe bronchopneumonia and responded to the usual therapy. When ready for discharge on the twelfth day the temperature rose suddenly to 38.8°C., and the stools became liquid.

Hgb. fell to 9.2 gm./100 cc. and WBC rose to 13.8 thousand with 75% polynuclear leukocytes, 14% lymphocytes, 9% monocytes, 1% basophiles, and 1% metamyelocytes. Urinalysis showed albuminuria but was otherwise within normal limits. The CO_2 combining power was 11 mEq./l. The nasopharyngeal culture yielded Esch. coli. Bilateral myringotomy was done and the discharge from both ears grew out Esch. coli. The stool culture was negative for organisms of the typhoid, paratyphoid, dysentery or salmonella groups.

A constant intravenous infusion was started with sixth molar sodium lactate, 5% dextrose in saline, and amigen. The diarrheal stools persisted and the fever remained elevated. On the 19th hospital day a bilateral mastoidectomy was performed. Hemorrhagic exudate was found in both mastoid areas which cultured Esch. coli. No improvement was noted following the operations and the body temperature rose to 41°C. Terminally there was marked abdominal distention and clinical evidence of a generalized bacteremia and peritonitis with beginning gangrene of the abdominal wall and extremities.

The infant expired on the 23rd hospital day. Permission for necropsy could not be obtained.

Case 2: M.McC. (45-993) Recovery from diarrhea contracted on the ward.

A four-week-old female infant was admitted with pyloric stenosis. A Fredet-Rammstedt operation was performed the day after admission with an uneventful course until the third post-operative day when loose stools were noted. Two days later the body temperature rose to 40.5°C., the diarrhea increased and bilateral otitis media was noted. Bilateral myringotomy released purulent material which cultured Esch. coli. At this time the nasopharyngeal culture yielded Esch. coli predominantly. The stool culture was negative for typhoid, paratyphoid, dysentery or salmonella organisms. The catheterized urine showed albuminuria and microscopic pyuria. The WBC rose to 25.5 thousand with 67% polynuclear leukocytes, 24% lymphocytes, 1% eosinophiles and 8% monocytes.

A constant intravenous infusion was begun with 5% glucose in saline, plasma, sixth molar sodium lactate and amigen. Sodium sulfadiazine and penicillin were given parenterally. The diazine level was maintained at 10 mg./100 cc. blood. The diarrhea persisted, the infant's condition became critical and remained so for the next week. Several transfusions of whole blood were given and a second constant intravenous infusion was necessary for parenteral fluid administration. Bloody discharge oozed from the nose, the stools were bloody and the baby vomited coffee-ground material. Vitamin K was administered with improvement and the abdominal distention was controlled with prostigmine. Ascorbic acid and calcium gluconate were given intravenously.

The stools improved gradually and a higher caloric intake was tolerated. Thereafter convalescence was uneventful although the weight gain was slow. The baby was discharged one month after the onset of the diarrhea with a weight of 3.0 kg.

Adequate bacteriologic studies were carried out in the critically ill babies with protracted diarrhea. A striking finding was the predominance of gram-negative organisms of the colon group which were cultured from the nasopharynx, the discharge from the ears, and the catheterized urine. Stool cultures were consistently negative for organisms of the typhoid, paratyphoid, dysentery or salmonella groups. The bacteriologic data together with other pertinent data are summarized in Table I. As the table shows, the diarrhea persisted for long periods in most of the infants, which necessitated a prolonged hospital stay.

TABLE I

BACTERIOLOGIC CULTURES—1945
INFANTS WITH PROTRACTED DIARRHEA OBSERVED ON WARD NOT OBTAINED BY HISTORY

Name Age	Nasopharynx	Ear Discharge	Catheterized Urine	Stool	Blood	Spinal Fluid	Miscellaneous	Classification	Days Diarrhea	Remarks
D.S. 7 wks.	Esch. coli	Esch. coli		neg.			Mastoids Esch. coli	severe	14	died
M.V. 15 mo.	beta s.		Esch. coli			neg.		severe	3	died
G.C. 3 mo.	Esch. coli	Esch. coli			neg.	neg.		severe	11	died
P.A.B. 2 days			Esch. coli	neg.				severe	9	died
J.S. 2 mo.	Staph. aureus	Esch. coli						severe	8	recovered
F.H. 16 mo.	H. influenzae non-typable pneumoncoccus 33	Staph. aureus						severe	6	recovered
M.W. 5 wks.		no culture	beta s. Esch. coli	neg.		neg.		severe	18	recovered
C.W. 2 mo.		Staph. aureus	neg.	neg.		neg.		severe	19	recovered
R.R. 5 mo.		Staph. aureus		neg.				severe	19	recovered
D.M. 4 wks.	Esch. coli	Esch. coli		neg.	neg.			severe	26	recovered
J.P. 2 wks.	Staph. aureus	Staph. aureus		neg.				severe	31	recovered
E.E. 6 mo.	Staph. aureus			neg.				severe	10	recovered
R.V. 6 wks.	Esch. coli			neg.				moderate	16	recovered
B.J. 9 mo.	Staph. aureus		gram-neg. bacilli			neg.	leg abscesses Staph. aureus	moderate	13	recovered
R.S. 9 mo.	H. influenzae Type B	neg.				H. influenzae Type B		moderate	18	recovered
C.R. 8 mo.	H. influenzae non-typable	Staph. aureus	Esch. coli			neg.		moderate	6	recovered
C.B. 8 mo.	alpha s.				neg.		leg abscesses Staph. aureus	moderate	6	recovered

CURRENT MANAGEMENT OF DIARRHEA

In the fall of 1947 all infants admitted to the Children's Hospital with diarrhea and those who developed the disease on the infant ward were housed in a separate isolation unit in another part of the building. Nurses and doctors who cared for the diarrheal infants did not come in contact with other patients on the infant ward, and strict isolation technic was instituted. All of the infants except a few private patients were treated in the following prescribed manner:

In order to establish the proper treatment on admission, infants with diarrhea (visualized on the ward and not by history) were classified into three groups:

(1) severe diarrhea, with vomiting, shock and diminished urinary output.
(2) moderate diarrhea, with vomiting.
(3) mild diarrhea, without vomiting on the ward.

Immediately after entry the infants with severe diarrhea, Group I, received intravenous saline to combat shock and stimulate circulation; 100 cc., for small infants and 200 cc., for larger babies. A constant intravenous drip was then established and if the infant was

in extreme shock, plasma was given; if time permitted whole blood was used in preference to plasma to combat the anemia which becomes apparent after hydration is attained in the severely ill infants. In general if the hemoglobin in the dehydrated infant was found to be 14.8 gm./100cc. or less, blood was used.

TABLE II

ORAL AMIGEN MIXTURE (DRY POWDER)*

Composition		
33% amigen (powdered casein hydrolysate)		
62% dextrose		
5% mineral salts	$CaCO_3$	1.30%
	basic $MgCO_3$	0.305%
	KCl	1.12%
	NaCl	0.84%
	NaH_2PO_4	1.03%
	Na_2CO_3	0.205%
	Ferric ammonium citrate	0.20%
Vitamins/100 gm. dry powder		
Thiamine hydrochloride	1 mg.	
Riboflavin	2 mg.	
Niacin	10 mg.	
Ascorbic acid	50 mg.	
Percentage Composition of Minerals in the Oral Amigen Mixture (dry powder)		
Na	1.09%	
K	0.69%	
Ca	0.65%	
Mg	0.14%	
Fe	0.06%	
Cl	1.53%	
P	0.53%	
Undeterm.	0.31%	
	5.00%	
In a 10% Solution of Oral Amigen Mixture—mEq./l.		
Na	47.3	
K	17.6	
Ca	32.6	
Mg	11.3	
Fe	3.3	
Cl	43.1	
P	34.1	

* Kindly prepared by Dr. Warren M. Cox of Mead Johnson and Company.

Acidosis was corrected with intravenous sixth molar sodium lactate, one half the calculated dose immediately, and the remaining half within 12 hours. Unless anuria or marked oliguria was noted, intravenous amigen was then allowed to drip into the vein slowly; until recently a mixture of 2.5% amigen, 2.5% glucose, and 0.45% saline was used; during the last few months Hartmann's mixture* has proved equally satisfactory. If anuria was a problem, 10% glucose in water was given until diuresis was established, after which the amigen was started. The total parenteral fluid intake per day

* 3 1/3% amigen, 3 1/3% glucose, in 1/3 Ringer's lactate solution.

was calculated on the basis of 225 cc./kg. body weight for the first 24 hours; thereafter, the amount was regulated by the condition of the patient.

Oral feeding with a special amigen mixture devised to simulate the mineral, protein, and carbohydrate content of skim milk was begun as soon as possible. The special amigen mixture is tolerated long before a modified milk feeding can be retained. Within 12 to 24 hours after admission, the infant was offered a single small trial feeding of the amigen mixture by mouth. If the trial feeding was vomited, or if abdominal distention developed, no further feeding was offered for 12 hours; after the rest period another trial was made. As soon as oral feedings of the special amigen mixture were

TABLE III

RECOMMENDED THERAPY FOR INFANTS WITH SEVERE DIARRHEA

	Butler I.V.	Darrow I.V.	mEq./l. Hartmann[1] Amigen I.V.	Author[2] Amigen I.V.	Author Amigen Oral 10% solution	Milk
Na	30	122	72	93	47	27
Cl	22	104	52	88	43	33
K	20	35	4	2	18	40
Ca	0	0	8	5	33	61
P	5	0	20	13	31	52
Lactate	20	53	7.6	0*	0*	0
			Percentage Composition			
Protein	0†	0†	3.3	2.5	3.3	3.5
Glucose	10	5	3.3	2.5	6.2	4.7

* Sixth molar sodium lactate given separately.

† Amigen added later—usually after 48 hours.

[1] Hartmann—I.V. amigen, 3¼% amigen, 3¼% glucose, ⅓ Ringer's lactate solution.

[2] Author—I.V. amigen: 2½% amigen, 2½% glucose, 0.45% saline.

tolerated, the baby was fed regularly every three hours; the total amount of oral amigen offered was calculated on the basis of 200 cc./kg. body weight/24 hours of the 10% solution. With acceptance of the oral amigen, in all but the most intractable cases intravenous feeding could be discontinued within 24 to 48 hours.

The original oral amigen mixture prepared five years ago was designed to simulate the composition of skim milk, with additional sodium chloride; shortly thereafter the mineral content was reduced. The present mixture as shown in Table II contains 33% dry powdered amigen, 62% glucose, 5% added mineral salts, and vitamins B and C. When fed in 10% solution, the mixture is acceptable to young infants, is fat-free, approximates the protein and sugar content of milk, and contains about half the concentration of calcium, potassium and phosphorus found in milk, with somewhat higher sodium and chloride levels. A practical advantage to the use of early oral amigen is the elimination of prolonged intravenous administration which is not only time consuming but often technically difficult; and in addition the oral route is safer for the administration of potassium. In Table III the composition of the various intravenous solutions proposed for the treatment of dehydration and acidosis in diarrhea is summarized together with the composition of oral amigen and milk.

Vitamin K was administered to all infants intramuscularly immediately after entry

and for several days thereafter. Vitamins B and C in high dosage were added to the drip as long as intravenous amigen was continued since the intravenous amigen solution lacks vitamins. If prolonged intravenous feeding was obligatory, calcium gluconate was added to the drip to guard against tetany.

When the stools improved in number, but long before cessation of watery stools, alternate feedings of amigen and nutramigen were given to introduce a small amount of fat (2%). If tolerated, at the end of two days, nutramigen was fed which represented a normal caloric intake as well as a normal fat level. Then nutramigen and evaporated milk feedings were alternated to introduce undigested casein for the first time. It was interesting that this transition point was the most troublesome, and in a few infants it was necessary to revert to the nutramigen feedings for a longer time.

Since many of the infants had severe complicating infections such as bronchopneumonia, purulent otitis media, or pyuria, it was customary to treat empirically with sulfadiazine and penicillin on admission until the bacteriologic cultures indicated the etiologic organisms. Oxygen was used when indicated.

Treatment of Parenteral Diarrhea With Streptomycin

In spite of the above regimen some of the infants did not progress satisfactorily; that is, the diarrhea recurred after a period of improvement or was intractable, with fatal results. Predominance of gram-negative organisms of the colon group in bacteriologic cultures was still noted in spite of improvements in technic on the isolated ward, which might have been expected to reduce the sources of direct contamination.

With the availability of streptomycin in 1946 specific therapy for the underlying infection could be offered to infants with diarrhea harboring gram-negative organisms. Streptomycin passes through the gastro-intestinal wall with great difficulty. Elias and Durso[54] found no demonstrable streptomycin in the blood after the oral administration of 4 million units (4 gm.) per day; 64% was eliminated in the stools and approximately 1% was recovered in the urine. When the same amount of drug was given intravenously, only a trace was recovered in the stools. Similar results were recorded by Adcock and Hetting,[55] Buggs,[56] and Anderson and Jewell.[57] After treatment of a patient infected with E. typhosa by both parenteral and oral streptomycin, Reimann et al[58] recovered streptomycin from the stools in amounts more than sufficient to suppress the growth of E. typhosa and Esch. coli in the feces. They suggested that both parenteral and oral streptomycin be used in the treatment of typhoid: the first to control systemic and urinary tract infection; the latter, to sterilize the feces, prevent reinfection, and to avoid the carrier state. It would seem appropriate then to treat infantile diarrhea in which gram-negative organisms are found both in the gastro-intestinal tract and systemically by the oral and parenteral routes.

The bacteriologic cultures of the first 17 infants treated with streptomycin are tabulated in Table IV, as well as the duration of the diarrhea. Since the bacteriologic cultures suggested systemic invasion of organisms of the colon group, the streptomycin was given intramuscularly as well as orally; and because of the possible toxicity, the use of the drug was limited to those infants who were critically ill and who had failed to respond to the usual measures, including treatment with sulfadiazine and penicillin.

Eight infants with intractable diarrhea, who had not responded to the conventional treatment, received streptomycin for ten days; the drug was given in divided doses every three hours; 0.5 gm. was injected intramuscularly and 0.5 gm. was given orally per 24 hours. Dissolved in a small amount of saline and offered orally in 15 cc. of the amigen

TABLE IV

BACTERIOLOGIC CULTURES—1947
INFANTS WITH DIARRHEA TREATED WITH STREPTOMYCIN LATE IN THE COURSE

Name Age	Nasopharynx	Ear Discharge	Catheterized Urine	Stool	Blood	Spinal Fluid	Classification	Days Diarrhea	Remarks
S.M. 2 mos.				neg.	neg.		severe	24	recovered
D.W. 3 mos.	Esch. coli		Esch. coli	neg.	neg.		severe	14	recovered
L.R. 2 mos.	Esch. coli		Esch. coli	neg.		neg.	severe	19	recovered
F.R. 3 mos.	Pneumococcus 3 beta s.		Esch. coli	neg.	neg.	neg.	severe	15	recovered
P.G. 4 mos.	beta s.		Esch. coli		neg.	neg.	severe	12	recovered
L.H. 6 mos.	Esch. coli			neg.			severe	12	recovered
G.C. 8 mos.	Esch. coli		Esch. coli	neg.			severe	12	recovered
G. Co. 4 mos.	beta s.		Esch. coli	neg.	neg.		moderate	11	recovered
	INFANTS TREATED WITH STREPTOMYCIN DURING FIRST WEEK OF DIARRHEA AFTER IDENTIFICATION OF ETIOLOGIC ORGANISMS								
W.B. 3 mos.	beta s. Esch. coli			neg.			severe	5	recovered
A.C. 6 mos.	H. influenzae Type B		Esch. coli	neg.	neg.	neg.	severe	7	recovered
R.B. 3 wks.	Staph. aureus		Esch. coli	neg.			severe	7	recovered
D.B. 3 mos.	Esch. coli			neg.			moderate	8	recovered
	INFANTS TREATED WITH STREPTOMYCIN ON FIRST HOSPITAL DAY OF DIARRHEA BEFORE IDENTIFICATION OF ETIOLOGIC ORGANISMS								
D.P. 3 mos.	beta s. Esch. coli	beta s.	neg.	neg.	neg.		severe	8	recovered
J.R. 7 wks.	Esch. coli	Esch. coli					severe	6	recovered
C.F. 6 mos.	Esch. coli		neg.		neg.		severe	5	recovered
E.B. 5 wks.	Esch. coli		Esch. coli		neg.		moderate	5	recovered
D.P. 6 wks.	Staph. aureus		neg.		neg.		mild	5	recovered

mixture, the drug is acceptable. Although difficulty in oral administration was expected, none was actually encountered, since even the critically ill infants could tolerate this small amount of material by mouth. Occasionally the first single oral dose was vomited, but persistent vomiting of the drug did not occur.

The response to streptomycin therapy was immediate and most gratifying. (See Table IV for the bacteriologic data and duration of the diarrhea.) The body temperature fell promptly and the character of the stools improved within a short time; the voluminous

watery stools usually ceased within 24 to 48 hours. The infants showed striking improvement clinically, and accepted feedings of higher caloric content within 24 hours after initiation of the streptomycin. The course of two of the infants in this group, F.R. and L.R., is shown graphically in Charts I and II, and the protocols are presented in detail below.

Later, as success with the drug was demonstrated, streptomycin was given to four seriously ill infants during the first week of hospitalization as soon as cultures indicated the predominance of gram-negative organisms. Chart III represents the course of one patient, A.C., of this group. See Table IV for the bacteriologic cultures and the duration of the diarrhea. Shortly thereafter, five infants were treated with streptomycin on admission to the hospital after the cultures were taken but before the results were available. The clinical course of one patient, J.R., is illustrated in Chart IV. The results with the early use of streptomycin were again most gratifying; the data suggested that the administration of the drug immediately after admission shortened the hospital stay, presumably by prevention of the complications due to the systemic spread of the gram-negative bacteria.

Protocols of four infants with diarrhea who were treated with streptomycin follow:

Case 3: (#2501) F.R. Protocol of case illustrated in Chart I.

A three-month-old Mexican infant, who had been well until two days previously when the family physician diagnosed an upper respiratory infection, was admitted to the Children's Hospital. The night before entry, the mother noted generalized "shaking" of the extremities, irritability, and a temperature of 41.6°C. The infant was given penicillin in oil and a saline clysis in the home. There had been no vomiting during the short illness and the bowel movements were normal.

The family history was non-contributory. The baby had been a full-term infant and weighed 3.75 kg. at birth; the neonatal and subsequent courses were uneventful.

Physical examination revealed a critically ill moderately dehydrated infant with a grayish pallor. The fontanelle was depressed, but the skin showed fair turgor. The body temperature was 41.3°C., and weight was 5.75 kg. Respiration was rapid, about 70/min. The percussion note was moderately dull over the right posterior lung field with fine rales scattered over this area. The heart was not enlarged to percussion, no murmurs were noted and the rate was 172. The liver was enlarged, but the spleen was not palpable. Meningeal signs were not present.

Roentgen examination of the chest was consistent with bronchopneumonia. The nasopharyngeal culture yielded pneumonococcus, Type III and rare beta s. The blood culture was sterile. Hgb. was 9.4 gm./100 cc.; RBC was 3.9 million; WBC was 9.2 thousand with 55% polynuclear leukocytes, 40% lymphocytes, 4% monocytes and 1% eosinophiles. The CO_2 combining power was 11 mEq./l. Urinalysis was within normal limits. The cerebrospinal fluid contained two leukocytes; protein, 30 mg./100 cc. fluid; sugar 94 mg./100 cc.; chloride 139 mEq./l. and the culture was sterile. The Mantoux test with 0.1 mg. O.T. was negative as was the blood Kahn test. A stool culture yielded no organisms of the typhoid, paratyphoid, dysentery or salmonella groups.

The patient was placed in an oxygen tent and given penicillin and digifolin. A constant intravenous infusion was started with sixth molar sodium lactate and amigen, and continued for two days. The temperature fell rapidly to normal and the next morning, with adequate urinary secretion, sodium sulfadiazine was started subcutaneously. The baby was kept in an oxygen tent for four days. Although offered a standard evaporated milk feeding it was accepted poorly. The stools were normal. On the third hospital day the body temperature rose to 39.4°C. and remained elevated for the next three weeks; on the ninth day, diarrhea developed which persisted. During the second week, the cerebrospinal fluid was normal and the culture was sterile. Several blood counts revealed a moderate secondary anemia with Hgb., 10.1 gm./100 cc. and RBC, 3.7 million.

Oral feedings were discontinued and a constant intravenous infusion was started again; sixth molar sodium lactate and amigen were allowed to drip in continuously for eight days, interrupted for one day, and recontinued for another four days. Three transfusions were given which brought Hgb. up to 14.5 gm./100 cc. Repeated urinalyses during this period were within normal limits. The diarrhea was intractable with 10 to 12 watery stools a day, and the temperature ranged

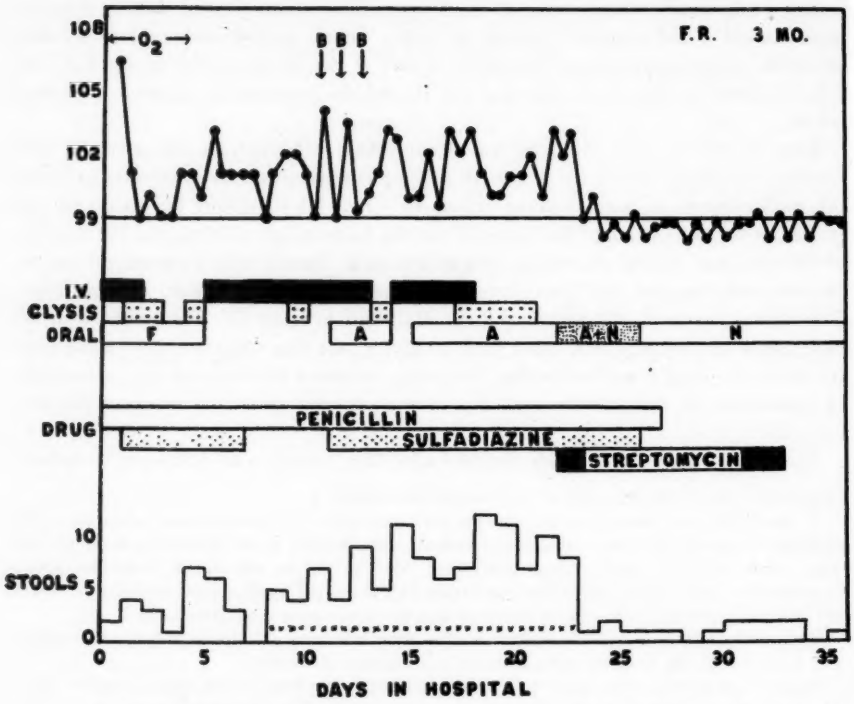


CHART I. The results of oral and intramuscular streptomycin late in the course of intractable diarrhea.

CODE*

O_2 = oxygen therapy
B = blood transfusion
P = plasma transfusion
F = evaporated milk formula—20 calories per ounce
A = special oral amigen mixture—10% solution
N = Nutramigen—20 calories per ounce
X in stool column = large liquid stools which caused dehydration

* The same code applies to the other three charts.

between 38.3° and 40°C. The infant's condition grew steadily worse and hydration could not be maintained satisfactorily even with the constant intravenous drip and oral amigen by mouth. Penicillin and sulfadiazine were given throughout this period, except for a short interruption of the sulfa drug.

Three weeks after entry a roentgenogram of the chest showed persistence of the bronchopneumonic lesions but excluded progression to effusion or empyema. The cerebrospinal fluid was again normal with a sterile culture; the blood culture was negative. At this point the nasopharyngeal culture yielded Esch. coli. The catheterized urine showed 5 to 50 leukocytes per high power field and three plus albumin, but the culture was sterile. The sulfa drug level throughout the first three weeks ranged between 6 and 12 mg./100 cc. blood. Repeated stool cultures were negative for organisms of the typhoid, paratyphoid, dysentery or salmonella groups.

Because of the unsuccessful course, streptomycin was given, 0.5 gm. orally and 0.5 gm. parenterally daily in divided doses for ten days.

The temperature fell immediately and within 36 hours the watery stools had ceased completely.

The clinical condition of the baby improved markedly and a higher caloric feeding was accepted at once. Hydration was maintained by oral feeding even though the feedings had to be given for four days with a dropper. A catheterized urine obtained after the course of streptomycin just before discharge from the hospital contained no albumin and was essentially negative microscopically; however, culture yielded colonies too numerous to count of a gram-negative rod of the coliform group.

The baby gained slowly and was discharged three days after the streptomycin was discontinued with a body weight of 5.3 kg.

Case 4: L.R. (#2528) Protocol of case illustrated in Chart II.

A two-month-old infant was admitted to the Children's Hospital. Ten days before admission

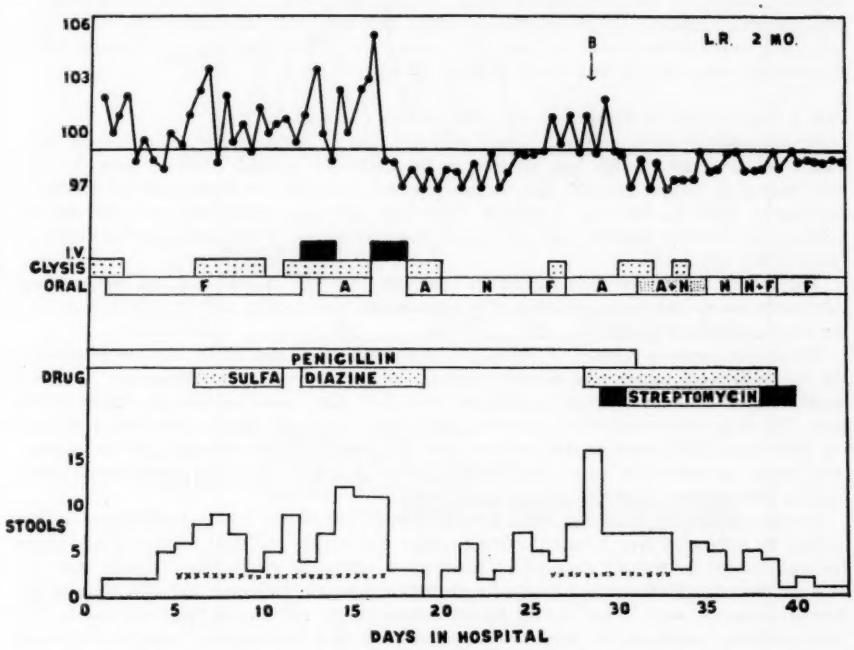


CHART II. The results of treatment with oral and intramuscular streptomycin in severe recurrent diarrhea. Code explained under Chart I.

she had developed a cough and was treated by her private physician with penicillin drops in the formula. Seven days before admission anorexia was noted.

The past history and family history were irrelevant.

On admission physical examination showed an acutely ill, well-developed, well-nourished Mexican female infant, irritable, but in no distress. The body weight was 4 kg., Hgb. was 13 gm./100 cc. WBC was 11.5 thousand with 44% polynuclear leukocytes, 52% lymphocytes and 4% monocytes. Urinalysis was within normal limits. The nasopharyngeal culture grew out hemolytic Staph. aureus. A lumbar puncture revealed normal manometrics; the spinal fluid showed no cells, protein 33 mg./100 cc., sugar 83 mg./100 cc. and chloride 124 mEq./l.; culture of the spinal fluid was negative. The blood Kahn test was negative.

The lung fields were clear by roentgenogram, but the diaphragms were low. A diagnosis of bronchopneumonia was made. With penicillin therapy the baby seemed to improve until the fifth hospital day, when the temperature rose and diarrhea developed. The CO_2 combining power was

found to be 14 mEq./l. Repeated urinalyses remained within normal limits. The diarrhea persisted and in spite of clyses, the infant became so dehydrated that, at the end of the second week a constant intravenous infusion was begun with sixth molar sodium lactate and amigen. Penicillin and sulfadiazine were continued throughout. Shortly thereafter oral amigen was begun. The body temperature fell to normal and within a few days the diarrhea was controlled. However, about ten days later severe diarrhea recurred with as many as 16 stools a day and the temperature rose again. The catheterized urine at this time showed microscopic pyuria and the urine culture grew out Esch. coli in colonies too numerous to count. Repeated stool cultures were negative for organisms of the typhoid, paratyphoid, dysentery or salmonella groups. Streptomycin was given both intramuscularly and orally, 0.5 gm. daily by each route, for the next ten days. Hgb. fell to 10.2 gm./100 cc. and a transfusion was given. Therafter, body temperature fell and the stools improved rapidly in character. Higher caloric feedings were instituted and the infant made an uncomplicated recovery. At the conclusion of the treatment with streptomycin the catheterized urine was within normal limits and the urine culture was sterile. The baby was discharged from the hospital on the 42nd day with a body weight of 3.9 kg.

Case 5: A.C. (#3273) Protocol of case illustrated in Chart III.

A six-month-old Mexican female infant who had been ill for a month with recurrent fever, cough, vomiting and diarrhea was admitted to the Children's Hospital. For two weeks she had been treated in another hospital with sulfadiazine and penicillin for bronchopneumonia; before discharge a mild diarrhea had developed. Four days later the diarrhea recurred and she was admitted to a different hospital; since the infant's condition became critical transfer to the Children's Hospital was requested.

The family history was non-contributory. Delivery had been normal and the neonatal and subsequent course had been uneventful. The birth weight was 3.4 kg. and the baby had doubled her weight within five months.

Physical examination revealed a critically ill, marasmic, dehydrated infant with severe acidosis; the eye balls were sunken and deviated upwards and the fontanelle was depressed. The body weight was 5 kg. Both tympanic membranes were dull. There was questionable rigidity of the neck. The lungs were resonant to percussion, with many coarse and crepitant rales heard throughout both lung fields, more marked on the right. The heart was not enlarged and no murmurs were heard. No masses or organs were palpated in the abdomen. There was no peripheral edema and the reflexes were hypoactive and equal bilaterally.

Roentgen examination of the chest revealed bronchopneumonia. The nasopharyngeal culture yielded H. influenzae, type B, and the blood culture was sterile. The stool cultures were negative for organisms of the typhoid, paratyphoid, dysentery or salmonella groups. On admission Hgb. was 11.9 gm./100 cc.; WBC was 8.5 thousand with 70% polynuclear leukocytes and 30% lymphocytes. Several urinalyses were within normal limits; culture of the catheterized urine was sterile. The CO_2 combining power was 10 mEq./l. The cerebrospinal fluid contained five cells per cmm. with a negative Pandy test, and the culture was sterile. The Mantoux test with 0.1 mg. O.T. was negative.

The body temperature which was normal on admission, rose shortly thereafter to 38.9°C. and persisted between 38.9° and 40.3°C. until the fifth day.

Soon after entry penicillin and sodium sulfadiazine were given. A constant intravenous infusion was begun with saline followed by sixth molar sodium lactate. On the second, third and fourth hospital days, transfusions of whole blood were given. Hgb. rose to 18.3 gm./100 cc. with little change in WBC.

Twelve hours after admission oral amigen was offered and was retained without vomiting. The intravenous drip was discontinued after three days and clyses of 5% glucose in saline were given to combat persistent dehydration. When the nasopharyngeal culture indicated that H. influenzae, type B, might be the etiologic agent, streptomycin was started on the fifth hospital day; 0.5 gm. was given orally and 0.5 gm. intramuscularly in divided doses daily for ten days. Soon after streptomycin was started the temperature dropped with immediate cessation of the voluminous watery stools, and within 24 hours the baby accepted high caloric feedings.

A second roentgenogram of the chest, taken a week later, showed that the pathologic lesions in

the lungs had cleared. After the streptomycin therapy the catheterized urine showed microscopic pyuria and the culture yielded B. aerogenes with colonies too numerous to count.

The course thereafter was uneventful with a rapid increase in caloric intake. The baby was discharged from the hospital on the 17th day with a weight of 5.5 kg.

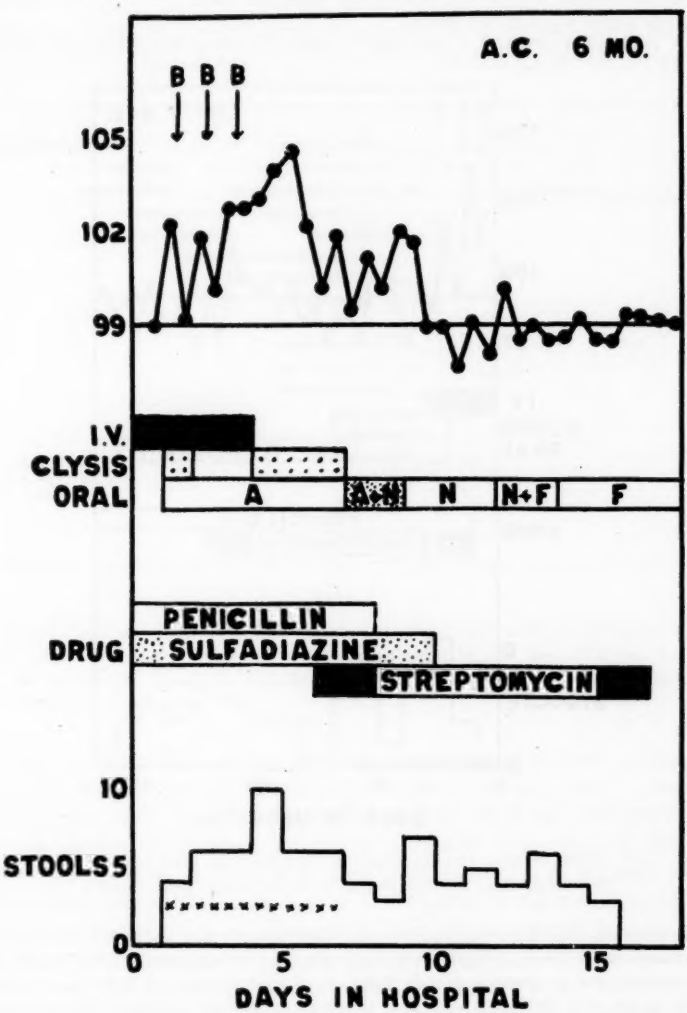


CHART III. The results of oral and intramuscular streptomycin early in the course of diarrhea. Treatment started as soon as gram-negative organisms were recovered from bacteriologic cultures. Code explained under Chart I.

Case 6 J.R. (#3800) Protocol of case illustrated in Chart IV.

A seven-week-old infant, admitted to the Children's Hospital, had been born prematurely and weighed 1.2 kg. at birth. The neonatal course was uncomplicated. The infant thrived in an

incubator and was discharged from the maternity hospital at five weeks of age with a weight of 2 kg. During the first ten days at home there was moderate regurgitation in spite of several changes in the formula. Irritability was noted four days before admission; two days before entry body temperature rose to 38.9°C. vomiting occurred and there were 10 to 12 loose stools daily. On the day of admission the diarrhea increased and the baby lapsed into shock.

The family history was non-contributory.

Physical examination revealed a very small critically ill infant dehydrated, with ashen pallor

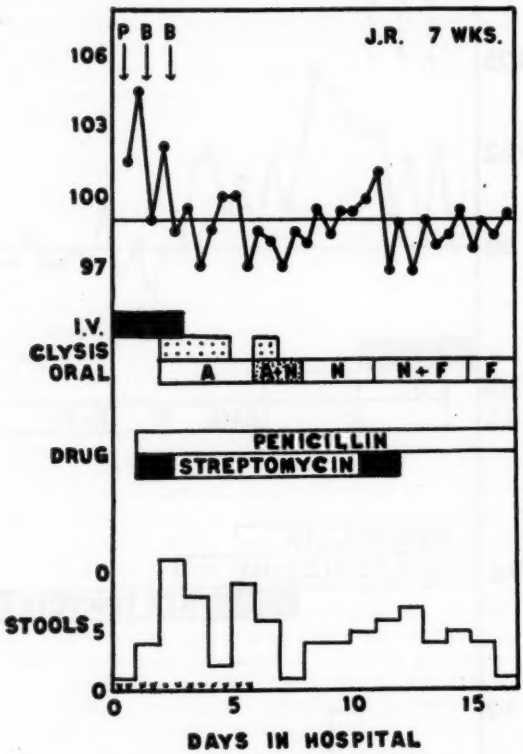


CHART IV. The results of oral and intramuscular streptomycin given on admission and before determination of the bacteriology. Code explained under Chart I.

and slight cyanosis. The baby weighed 1.9 kg. The fontanel was depressed, the cry was very weak, and respirations were irregular with slight grunting on expiration. There was no evidence of overt infection; the ear drums were dull. Hgb. was 10.2 gm./100 cc. and WBC was 12.4 thousand, with 65% polynuclear leukocytes and 35% lymphocytes. Routine urinalysis showed heavy albuminuria and 6 to 10 pus cells per high power field with an occasional fine granular cast. The nasopharyngeal culture grew out Esch. coli predominantly.

A constant intravenous infusion was begun with saline, plasma, sixth molar sodium lactate and amigen. Vitamin K and penicillin were administered. Streptomycin was given both intramuscularly and orally, 0.5 gm. daily by each route for 12 days. Transfusions of whole blood were given and within 36 hours after entry oral amigen was started by mouth. The body temperature fell rapidly following hydration. On the third hospital day, a right myringotomy produced purulent discharge, which ceased a few days later. Culture of the aural discharge grew out Esch. coli. Three days after

streptomycin was started, the stools improved markedly and higher caloric feedings were accepted on the seventh hospital day. Thereafter the infant made an uneventful recovery. Shortly before discharge Hgb. was found to be 14.3 gm./100 cc. WBC was 14.4 thousand and a routine urinalaysis was within normal limits. On discharge from the hospital on the 17th day the infant weighed 2.3 kg.

In Chart V the results of treatment with streptomycin of 17 critically ill infants with diarrhea are shown. The initiation of treatment is represented as the central point, with

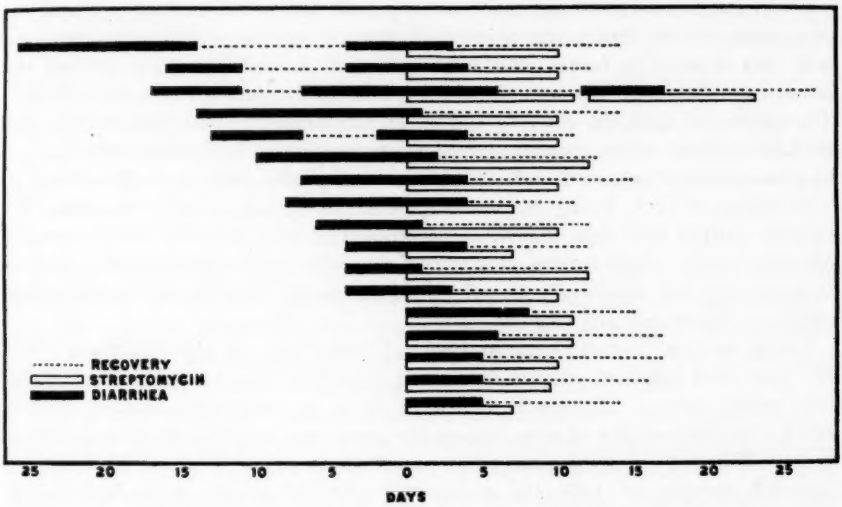


CHART V. Results of streptomycin in the treatment of seventeen critically ill infants with diarrhea. The initiation of treatment is represented as the center point (zero). The solid black bar indicates observed diarrhea on the ward; the open bar treatment with streptomycin; and the dotted line the recovery phase from the diarrhea.

the duration of observed diarrhea on the ward charted toward the left and the recovery phase plotted toward the right. It is apparent from the chart that treatment with streptomycin effectively shortened the hospital stay of all of the patients; in the five infants who received streptomycin directly on admission to the hospital, the diarrhea ceased within a few days. The immediate cessation of diarrhea is all the more remarkable since the patients received oral amigen early in the course of the disease, which tends to result in looser stools than those which result from evaporated milk feedings.

After these preliminary observations on the seriously ill patients were made with the use of both oral and intramuscular drug administration, it was felt that the action of oral streptomycin alone should be studied. It seemed desirable to learn whether oral streptomycin alone given early in the course of diarrhea would prevent the more serious complications seen in the protracted cases, and enable treatment of the patients with diarrhea from the Outpatient Department.

Plans were made to withhold streptomycin from every other patient so that these untreated babies could serve as controls. The plan had to be discarded soon after it was put into operation because many of the control infants became so seriously ill that

streptomycin could not justifiably be withheld. Most of the critically ill babies received the drug both orally and intramuscularly, so only the less seriously ill infants were carried on oral drug administration only. The data obtained from the additional patients treated with streptomycin were like that presented in Chart V; the results supported the previous conclusions and in the interest of brevity need not be graphed.

Morbidity and Mortality Statistics

Under the circumstances, untreated control patients from 1947 were not available for comparison with the infants who received streptomycin, but the results may be compared with data obtained in former years in this hospital. According to statistics from the record room there were 133 cases of infantile parenteral diarrhea in 1943 with 15 deaths. The uncorrected mortality was 11% and the corrected mortality 7%. Sulfa therapy was available to these infants, parenteral fluid reconstitution was furnished by 5% glucose in saline and sixth molar sodium lactate solution, and protein milk was used for feeding.

In March of 1945, during the severe epidemic on the infant ward, 41 infants developed diarrhea with eight deaths; an uncorrected mortality of 20% and a corrected mortality of 7%. These infants were treated with sulfa drugs and penicillin, received amigen orally and parenterally as well as saline, glucose, sixth molar sodium lactate solution, calcium salts and vitamins.

During the latter part of December 1946 and through the first eight months of 1947, 80 infants with parenteral diarrhea were cared for in the isolated diarrhea ward. Forty-four infants received streptomycin with three deaths, an uncorrected mortality of 7% and a corrected mortality of zero; among this group were most of the seriously ill patients.* Thirty-six infants did not receive streptomycin and six of them died; an uncorrected mortality of 16% and a corrected mortality of 3% (one death). The mortality of 3% was represented by a four-month-old infant moribund on admission, who died three days later. Necropsy showed bronchopneumonia and the post-mortem blood culture was positive for Esch. coli. The baby was admitted early in January of 1947 and did not receive streptomycin, because at that time the supply was so limited treatment was withheld until cultures identified gram-negative organisms. It is possible that this infant could have been saved with the drug.

In order to arrive at a correction of the mortality the following three deaths in 1947 were not attributed to failure of streptomycin in parenteral diarrhea:

1. A one-month-old infant, moribund on admission, died eight hours after admission and autopsy showed acute gastro-enteritis.
2. A one-day-old infant died of intestinal obstuction and bronchopneumonia following surgery for repair of a large omphalocele 6 cm. in diameter. At necropsy a volvulus was found caused by a congenital band which arose from the bladder. Bilateral hydronephrosis and pyelonephritis were also present.
3. A three-month-old infant with diarrhea had shown improvement when intestinal obstruction developed. Death occurred two weeks later and necropsy showed early bronchopneumonia and hemorrhage into the adrenals.

---

* In the earlier months of the study a few seriously ill infants were included in the control group; some babies died a few hours after admission and some had congenital anomalies incompatible with survival; later on all seriously ill infants received streptomycin.

In the control patients in 1947 who did not receive streptomycin, the mortality was corrected by exclusion of five deaths as follows:

1. A seven-week-old infant was admitted with a congenital heart and died 25 minutes after admission. The post-mortem examination revealed cardiac hypertrophy.
2. A 5½-month-old infant admitted with a Hgb., 2.2 gms./100 cc., and RBC, 0.74 million, died one hour after admission. At necropsy severe anemia was found and the post-mortem cultures were negative.
3. A two-month-old infant jaundiced since birth developed terminal diarrhea. Autopsy confirmed the clinical impression of an atresia of the extrahepatic bile ducts with absence of the gallbladder.
4. A seven-month-old infant admitted in extremis died nine hours after admission. Post-mortem examination showed pulmonary atelectasis and focal hemorrhages.
5. A ten-month-old infant with a marked pectus excavatum and a neurologic disorder died 20 hours after admission. Necropsy showed acute focal pneumonitis and gastro-enteritis.

Urinary Changes

Urinary changes were noted in most of the infants with parenteral diarrhea. The more seriously ill infants showed gross or microscopic pyuria in catheterized specimens. Cultures were planted immediately after catheterization to prevent multiplication of organisms on standing; for the most part colonies of gram-negative organisms of the colon group too numerous to count were grown from the catheterized urines.

In some infants the gross pyuria and positive cultures for Esch. coli disappeared after streptomycin treatment, but this was not invariably true. The infants all recovered and it seemed that the pyuria and bacilluria represented temporary disturbances of the kidney rather than genito-urinary tract infections. In several infants follow-up studies later revealed normal urine, a normal blood non-protein nitrogen and a normal urinary tract on intravenous pyelography.

Discussion

The effective dose of streptomycin for the treatment of infantile diarrhea was found to be 0.5 gm. intramuscularly and 0.5 gm. orally per day for 7 to 10 days. For premature and immature infants half this dosage is recommended. No evidence of toxicity to streptomycin was noted in any of the patients. Toxicity would be expected only from the drug given parenterally as the extremely small amount absorbed from the intestinal tract could hardly cause untoward reactions. Reimann et al.[58] with a dose of 1 million units (1 gm.) of oral streptomycin daily in an adult were able to obtain a concentration of the drug in the feces that suppressed the growth of E. typhosa and Esch. coli. In our hands 0.5 gm. of oral streptomycin given daily to diarrheal infants resulted in stools which were sterile on bacteriologic culture.

After the above results were obtained an abstract of the work of Aquirre, Aguayo, and Lazaro[59] came to the authors' attention. Eight infants with diarrhea in whom paracolon bacillus was recovered from the stools, were treated with injections of streptomycin, 55,000 (0.055 gm.) to 160,000 units (0.16 gm.)/kg. body weight/day. There were two deaths in the series. 100,000 units (0.1 gm.)/kg./day were recommended by these investigators in cases of moderate severity and 150,000 units (0.15 gm.)/kg./day for seriously ill infants. Recently Pulaski and Anspacher[60] reported the

results of treatment in a small series of infants with diarrhea using large daily doses of streptomycin, 0.1 to 0.6 gm./kg. body weight. Although they hesitated to draw conclusions from the small number of infants treated, they recommended 0.5 gm./kg. as the minimal daily dose for diarrheal infants and suggested 1 gm./kg. as the optimum dose in the critically ill baby.

Summary

In a severe epidemic of infantile diarrhea in 1945 and subsequently, bacteriologic cultures of the nasopharynx and the catheterized urine showed a predominance of gram-negative organisms of the colon group.

The response of seriously ill infants with parenteral diarrhea to streptomycin was dramatic, presumably because of the specific action of the drug against the gram-negative organisms. Streptomycin was used both orally and intramuscularly in the later stages of the disease.

Suggestions are offered for fluid and electrolyte replacement by means of an oral amigen mixture, which permits the introduction of potassium, calcium, and nitrogen as well as sodium and chloride by mouth shortly after admission.

The use of streptomycin and the oral amigen mixture, as an adjunct to the customary routine employed in previous years, effectively shortened the hospital stay, decreased the amount of intravenous therapy, and reduced the mortality. During the eight month period of observation no deaths were encountered which could be attributed to diarrhea.

References

1. Moro, E., Über Enterale Infection bei Sauglingen, Monatschr. f. Kindh. **22**:273, 1921.
2. Plantenga, B. P. B., Die Kolitoxicose des Sauglings, Geneesk. Gids. **5**:721, 1927.
3. Ibid. Jahrb. f. Kinderh. **121**:156, 1928.
4. Ibid. Nederl. maandschr. v. geneesk. **17**:69, 1930.
5. Ibid. Jahrb. f. Kinderh. **129**:253, 1930.
6. Howland, J., Mariott, W. M., Acidosis occurring with diarrhea, Am. J. Dis. Child. **11**:309, 1916.
7. Marriott, W. M., Hartmann, A. F., and Senn, M. J. E., Observations on nature and treatment of diarrhea and associated systemic disturbances, J. Pediat. **3**:181, 1933.
8. Hartmann, A. F., Chemical changes occurring in body as result of certain diseases, and effects of diarrhea, vomiting, dehydration and oliguria on acid-base balance of plasma of infants with mastoiditis, Am. J. Dis. Child. **35**:955, 1928.
9. Dick, G. F., Dick, G. H., and Williams, J. L., Etiology of epidemic of enteritis associated with mastoiditis in infants, Am. J. Dis. Child. **35**:557, 1928.
10. Ensign, P., Hunter, C. A., Epidemic of diarrhea in newborn nursery caused by milk-borne epidemic in community, J. Pediat. **29**:620, 1946.
11. Lyon, G. M., Folsom, T. G., Epidemic diarrhea of newborn; clinico-epidemic, pathologic and therapeutic aspects, Am. J. Dis. Child. **61**:427, 1941.
12. Light, J. S., Hodes, H. L., Studies on epidemic diarrhea of newborn: isolation of filtrable agent causing diarrhea in calves, Am. J. Pub. Health **33**:1451, 1943.
13. Buddingh, G. J., Dodd, Katharine, Stomatitis and diarrhea of infants caused by hitherto unrecognized virus, J. Pediat. **25**:105, 1944.
14. Rice, J. L., Best, W. H., Frant, S., Abramson, H., Epidemic diarrhea of newborn; preliminary considerations on outbreaks of highly fatal diarrhea of undetermined etiology among newborn babies in hospital nurseries, J.A.M.A. **109**:475, 1937.
15. Frant, S., and Abramson, H., Epidemic diarrhea of newborn; control and prevention of outbreaks in hospital nurseries, J. Pediat. **11**:772, 1937.
16. Ibid. Epidemic diarrhea of newborn; epidemiology of outbreaks of highly fatal diarrhea among newborn babies in hospital nurseries, Am. J. Pub. Heath **28**:36, 1938.

17. Abramson, H., and Frant, S., Epidemic diarrhea of newborn; clinical consideration, Am. J. Dis. Child. **55**:1288, 1938.
18. Frant, S., Abramson, H., Epidemic diarrhea of newborn, Brennemann's Practice of Pediatrics, Vol. I, W. F. Prior Company, Inc., Hagerstown, Md., 1947, p. 19.
19. Dodd, Katharine, Round table discussions on infection in the newborn period, epidemic diarrhea of newborn infant from point of view of clinical investigator, J. Pediat. **30**:700, 1947.
20. Gamble, J. L., Chemical Anatomy, Physiology and Pathology of Extracellular Fluid; Lecture Syllabus, Harvard University Press, Cambridge, Mass., 1947.
21. Ibid., Carbonic Acid and Bicarbonate in Urine, J. Biol. Chem. **51**:295, 1922.
22. Gamble, J. L., Ross, S. G., and Tisdall, F. F., Metabolism of fixed base during fasting, J. Biol. Chem. **57**:633, 1923.
23. Gamble, J. L., Blackfan, K. D., and Hamilton, B., Diuretic action of acid producing salts, J. Clin. Investigation 1:359, 1925.
24. Gamble, J. L., McIver, M. A., Effects of pyloric obstruction in rabbits, J. Clin. Investigation 1:531, 1925.
25. Gamble, J. L., Ross, S. G., Factors in dehydration following pyloric obstruction, J. Clin. Investigation 1:403, 1925.
26. Gamble, J. L., Body fluid changes due to continued loss of external secretion of pancreas, J. Exper. Med. **48**:859, 1928.
27. Gamble, J. L., Fahey, K. R., Appleton, Janet, MacLachlan, Elsie, Congenital alkalosis with diarrhea, J. Pediat. **26**:509, 1945.
28. Gamble, J. L., Deficits in diarrhea, J. Pediat. **30**:488, 1947.
29. Marriott, W. M., Enteral and parenteral factors in causation of diarrhea, South M. J. **24**:278, 1931.
30. Marriott, W. M., Serious nutrition and digestive disturbances in infancy, Brennemann's Practice of Pediatrics, Vol. I, W. F. Prior Co., Hagerstown, Md., 1937, p. 1.
31. Butler, A. M., McKhann, C. F., and Gamble, J. L., Intracellular Fluid Loss in Diarrheal Disease, J. Pediat. **3**:84, 1933.
32. Butler, A. M., Acidosis or alkalosis in infants and children with gastro-intestinal disturbances, chronic nephritis, and diabetes mellitus, M. Clin. of North America, **18**:1205, 1935.
33. Ibid., Electrolyte and water balance, New England J. Med. **220**:827, 1939.
34. Butler, A. M., and Talbot, N. B., Medical progress; parenteral-fluid therapy. I. Estimation and provision of daily maintenance requirements, New England J. Med. **231**:585, 1944.
35. Ibid., II. Estimation of losses incident to starvation and dehydration with acidosis or alkalosis and provision of repair therapy, New England J. Med. **231**:621, 1944.
36. Guest, G. M., Rapoport, S., Changes in organic acid-soluble phosphorus of blood cells (especially diphosphoglyceric acid fraction) in different pathologic conditions; clinical and experimental studies, Am. J. Dis. Child **56**:942, 1938.
37. Ibid., Role of acid-soluble phosphorus compounds in red blood cells in experimental rickets, renal insufficiency, pyloric obstruction, gastroenteritis, ammonium chloride acidosis and diabetic acidosis, Am. J. Dis. Child **58**:1072, 1939.
38. Ibid., Acid-soluble phosphorus compounds of red blood cells in diabetic acidosis, Am. J. Dis. Child. **60**:450, 1940.
39. Guest, G. M., Rapoport, S., Organic acid-soluble phosphorus compounds of blood, Physiol. Rev. **21**:410, 1941.
40. Guest, G. M., Organic phosphates of blood and mineral metabolism in diabetic acidosis, Am. J. Dis. Child. **64**:401, 1942.
41. Darrow, D. C., and Yannet, H., Changes in distribution of body water accompanying increase and decrease in extracellular electrolyte, J. Clin. Investigation **14**:266, 1935.
42. Darrow, D. C., Medical progress; body fluid physiology; relation of tissue composition to problems of water and electrolyte balance, New England J. Med. **233**:91, 1945.
43. Ibid., Retention of electrolyte during recovery from severe dehydration due to diarrhea, J. Pediat. **28**:515, 1946.
44. Govan, C. D., Jr., Darrow, D. C., Use of potassium chloride in treatment of dehydration of diarrhea in infants, J. Pediat. **28**:541, 1946.

45. Hartmann, A. F. and Smyth, F. S. Chemical changes in body occurring as result of vomiting, Am. J. Dis. Child. **32**:1, 1926.
46. Ibid., Acidosis and dehydration, Colorado Med. **26**:373, 1929.
47. Hartmann, A. F., Senn, M. J. E., I. Studies in metabolism of sodium r-lactate; response of normal human subjects to intravenous injection of sodium r-lactate, J. Clin. Investigation **11**:327, 1932.
48. Ibid., II. Studies in metabolism of sodium r-lactate; response of human subjects with acidosis to intravenous injection of sodium r-lactate, J. Clin. Investigation **11**:337, 1932.
49. Ibid., III. Studies in metabolism of sodium r-lactate; response of human subjects with liver damage, disturbed water and mineral balance, and renal insufficiency to intravenous injection of sodium r-lactate, J. Clin. Investigation **11**:345, 1932.
50. Ibid., Round table conference on acidosis and alkalosis, J. Pediat. **5**:394, 1934.
51. Hartmann, A. F., Theory and practice of parenteral fluid administration, J.A.M.A. **103**:1349, 1934.
52. Hartmann, A. F., Perley, Anne M., Basman, J., Nelson, M. V., Asher, Cecile, Further observations on metabolism and clinical uses of sodium lactate, J. Pediat. **13**:692, 1938.
53. Weihl, Carl, Rapoport, S., Dodd, Katharine, Treatment of acute diarrhea in Cincinnati General Hospital during years 1944 and 1945, J. Pediat. **30**:45, 1947.
54. Elias, W. F., Durso, Jane, Blood, urine and fecal levels of streptomycin in treatment of human infections of E. typhosa, Science **101**:589, 1945.
55. Adcock, J. D., Hettig, R. A., Absorption, distribution, and excretion of streptomycin, Arch. Int. Med. **77**:179, 1946.
56. Buggs, C. W., Pilling, M. A., Bronstein, B., Hirshfeld, J. W., Absorption, distribution, and excretion of streptomycin, in man, J. Clin. Investigation **25**:94, 1946.
57. Anderson, D. G., Jewell, M., Absorption, excretion and toxicity of streptomycin in man, New England J. Med. **233**:485, 1945.
58. Reimann, H. A., Elias, W. F., Price, A. H., Streptomycin for typhoid, Pharmacologic study, J.A.M.A. **128**:175, 1945.
59. Aguirre, A., Aguayo, A., Benavides, L., Results of streptomycin treatment, in eight cases of diarrhea with Esch. coli and proteus in the stools, Boletin Medico del Hospital Infantil **14**:4, 1947.
60. Pulaski, E. J., Anspacher, W. H., Streptomycin therapy for certain infections of intestinal origin, New England J. Med. **237**:419, 1947.

SPANISH ABSTRACT

Tratamiento de la Diarrea Infantil con Streptomicina y Mezcla de Amigeno por Via Oral.

En una severa epidemia de diarrea infantil en 1945 se realizaron cultivos bacteriologicos de la naso-faringe y orina extraida por cateterismo los que dieron como resultado el predominio de organismos gram negativo del grupo colico.

La respuesta de muy severos casos de diarrea parenteral, en niños fue realmente dramatica con el uso de la streptomicina, problablemente debido a la accion especifica de la droga frente a los organismos gram negativo. La streptomocina fue usada por via oral y por via intramuscular en los ultimos estadios de la enfermedad.

Se sugirio el empleo de soluciones electroliticas por via oral con mezcla de amigeno lo cual permitio la introduccion de potasio y calcio, y nitrogeno asi como tambien cloruro de sodio por via oral inmediatamente despues de la admision de estos enfermos.

El uso de la streptomicina y de la mezcla de amigeno oral usada como rutina desde años anteriores, acorta efectivamente la estancia en el hospital de estos enfermos, disminuye la cantidad de terapeutica intravenosa y reduce notablement la mortalidad. Durante el periodo de ocho meses de observacion a que se refiere este trabajo, ninguna muerte puede ser referida a la diarrea como causa determinante.

4614 Sunset Blvd.

THE VOLUME OF EXTRACELLULAR BODY FLUIDS IN MALNUTRITION

By E. KERPEL-FRONIUS, M.D., AND S. KOVACH, M.D.
Pécs, Hungary

WASTING in starvation does not affect all the organs of the body in an equal measure (Voit[1]). This observation suggests the study of the composition of the body in infantile malnutrition. In analyzing this problem, our first endeavour was to get information about the distribution of body fluids in malnutrition. It was felt that extra and intracellular water may be sacrificed in different proportions in the process of wasting.

The volume of extra and intracellular fluids is remarkably constant in healthy adults (Lavietes[2]). In the infant, however, the process of growth itself is attended by a peculiar change in the distribution of body fluids; the amount of extracellular fluid was found to decrease during growth. This fact was first recognized for the human fetus by Harrison, Darrow and Yannet,[3] for the growing human infant and infantile animals by Kerpel-Fronius.[4] Recent determinations of radio-sodium space (Flexner and Fellers[5, 6]) and thiocyanate space in newborn and growing infants corroborated the statements of these early investigations, based on measurements of extra and intracellular minerals. The data of Fellers, Barnett, McNamara and Hare[6] show that the volume of extracellular fluid, expressed in percent of body weight, decreases progressively during infancy and childhood.

In the present study thiocyanate space was determined in 14 cases of severe malnutrition and in a number of healthy infants. The ages of the infants ranged between 3 and 12 months. Measured amounts of sodium thiocyanate were injected intravenously, and the distribution of the latter was determined one hour following administration. In this time the diffusion of thiocyanate seems to be complete.[2, 7, 8]

The results are summarized in Fig. 1.

Infants with weights ranging between 90% and 120% of the ideal weight are to be considered normal. The volume of extracellular fluid in this normal group of infants ranges between 27% and 35% of body weight, the higher values occurring in younger (black circles) the lower in older (white circles) infants. These values are in close agreement with the data of Fellers, Barnett et al.

The cases of malnutrition are found on the abscissa scale below 90%. The figures at the extreme left are the severest cases, half of their body weight being wasted.

It is clear from the figure that with increasing malnutrition the proportion of body weight consisting of extracellular water increases considerably. In the severest cases it can be concluded that the intracellular tissue and the fat content of the body suffer the heaviest loss as in starvation. This fact indicates that protoplasmic loss in severe malnutrition is even more extensive than is estimated from the proportion of actual to ideal weight of the patient.

It can be seen (Fig. 2) that the volume of extracellular fluid was diminished in the marantic infants. The remaining part of the body is, however, comparatively more wasted than the extracellular fluid compartment.

From the Department of Pediatrics, University of Pécs, Hungary.
(Received for publication May 9, 1948.)

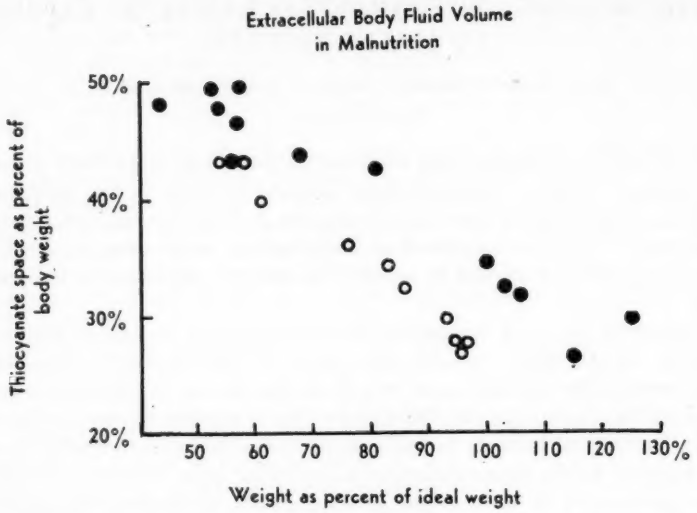


FIG. 1. The ordinate shows the thiocyanate space (extracellular fluids) in percent of body weight. The abscissa shows the extent of malnutrition as percent of the "ideal body weight" of healthy infants of the same age. White circles are older and black circles are younger infants.

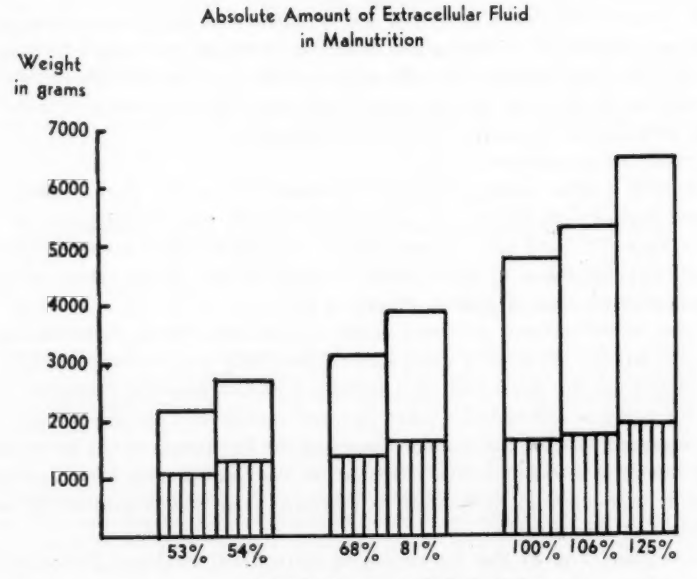


FIG. 2. Absolute amounts of extracellular water in seven three-month-old babies, their condition ranging from extreme malnutrition (left) to overweight (right). The height of each column represents the weight of the infant in grams. The blackened part of the column shows the amount of extracellular fluid in grams.

This disproportion in wasting leads to the increase in extracellular water in relation to actual body weight, as shown in Fig. 1.

As to the origin of the described disproportion in the loss of body weight in malnutrition, it should first be emphasized that frank edema was observed in none of the infants. Low protein values however were found in some of the cases. Two factors seem to be of some importance: 1. The skin is known to contain a much higher proportion of extracellular than intracellular fluid. As body surface decreases less in malnutrition than does body weight, a relative increase of extracellular water might be expected. 2. On the other hand, the mass of muscles, i.e. the system containing the largest proportion of intracellular water, is wasted to a great extent in such cases.

Conclusions

Extracellular body fluid volume, as measured by the thiocyanate method, was found to increase per kilo of weight considerably in malnutrition. In severe malnutrition nearly half of the body is made up of extracellular water. The absolute amount of the latter is, however, decreased, though proportionately to a smaller extent than fat and protoplasmic tissue. The amount of cellular tissue is consequently even smaller than indicated by the proportion of the actual weight of the marantic infant to the ideal weight of healthy infants of the same age. The greater hydrolability of marantic infants is thought to have some bearing on the described change in the distribution of body fluids.

References

1. Voit, C., Ueber die Verschiedenheiten Eiweisszersetzung Bein Hungern, Ztschr. Biol. **2**:307, 1866.
2. Lavietes, P. H., Bourdillon, J., and Klinghoffer, K. A., Volume of extracellular fluids of body, J. Clin. Investigation **15**:261, 1936.
3. Harrison, H. E., Darrow, D. C., and Yannet, H., Total electrolyte content of animals and its probable relation to distribution of body water, J. Biol. Chem. **113**:515, 1936.
4. Kerpel-Fronius, E., Über die Besonderheten der Salz- und Wasserverteilung im Sauglingskorper, Ztschr. f. Kinderh. **58**:726, 1937.
5. Flexner, L. B., Wilde, W. S., Proctor, V. K., Cowie, D. B., Voscugh, G. J., and Hellmann, L. M., Estimation of extracellular and total body water in newborn human infant with radioactive sodium and deuterium oxide, J. Pediat. **30**:13,1947.
6. Fellers, F., Barnett, H. H., McNamara, H., and Hare, K., Personal communication.
7. Mach, R. S., and Odier, J. Les liquides extra-cellulaires chez l'homme normal et chez les sujets traités par l'acétate de désoxycorticostérone, J. Suisse de Med. **26**:579, 1946.
8. Balint, P., Lazarovits, G., and Szarbo, G., A Szervezet Viztereinek Meghatározása. Orvosok Lapja, **13**:739, 1948.

Spanish Abstract

El Volumen del Fluido Extracelular en los Malnutridos

El volumen del liquido extracelular del cuerpo, medido por el metodo del tiocianato revela un aumento considerable por kilo de peso en los malnutridos.

En los casos severos de mala nutricion cerca de la mitad del peso del cuerpo esta constituida por el agua extracelular, la cantidad absoluta de ésta esta sin embargo disminuida proporcionalmente en menor extension que la grasa y los tejidos protoplasmaticos.

La cantidad de tenido celular es en consecuencia aun mas pequeña que la indicada por la proporcion del peso actual de los niños marasmaticos en relacion con el peso ideal de los niños sanos de la misma edad. La mayor hidrolabilidad de los niños marasmaticos esta en relacion con la condicion de los cambios en la distribucion de los fluidos del cuerpo.

Department of Pediatrics, University of Pécs

HEMOLYTIC STREPTOCOCCAL VAGINITIS IN CHILDREN

By PAUL L. BOISVERT, M.D. AND DWAIN N. WALCHER, M.D.
New Haven, Conn. and Indianapolis, Ind.

OUR attention was first focused on the probable relationship between hemolytic streptococci and vaginitis in children when in 1939 a 21-month-old-baby was examined in this clinic because of vaginal discharge. A stained smear of the discharge showed gram-negative diplococci which suggested to the examining physician the diagnosis of gonococcal vaginitis. On culture, however, a pure growth of hemolytic streptococci was obtained. No gonococcal colonies were present. The streptococci isolated from the vaginal discharge were Group A.

A study of our hospital in-patient records from 1928 through 1939 revealed five cases where a culture of the vaginal discharge yielded hemolytic str. The organisms were present in predominating numbers without other recognized pathogens, or in pure culture. The culture results apparently attracted little or no attenion at the time, for two of these children were discharged from this hospital with the diagnosis of gonococcal vaginitis, the diagnosis having been made on the basis of a stained smear. One of these children had scarlet fever and had hemolytic str. in the nose and throat. The other child had hemolytic str. in the nasopharynx without recognized evidence of streptococcal disease. It is our impression that these cases were misdiagnosed and are examples of hemolytic str. rather than gonococcal vaginitis. Unfortunately, it is too late to exclude a gonococcal infection. In those days culture media were inferior to those now in use, and the value of carbon dioxide in favoring the growth of the gonococcus was not recognized.

Qualitative studies on the organisms found in the vagina of children and adults by Hare,[1] Weinstein,[2] Hardy,[3] and Schaefer,[4] have shown that the hemolytic str. is occasionally present. Vaginitis resultant therefrom has not been reported in detail.

MATERIALS AND METHODS

This study is based upon the cultures taken on 286 patients seen on the Pediatric Inpatient Service from 1928 through 1945 and in the Pediatric Clinic from 1935 through 1945. Five hundred and twenty-four vaginal cultures were examined. There were 37 patients (12.9%) with hemolytic str., 33 with gonococci, and 11 with pneumococci. Nasopharyngeal cultures were obtained on 30 of the 37 patients with hemolytic streptococcal vaginitis.

Culture material was grown on rabbit's blood agar plates for about 18 hours at 37° C. Vaginal cultures were first grown in an atmosphere of 10% CO_2 in 1937. Thereafter this manner of culturing vaginal discharges was used routinely. Gentian violet plates were used in addition to rabbit's blood agar plates during the last year of the study.

CASE REPORTS

The marked variability in the histories encountered is illustrated by the three cases briefly summarized.

From the Department of Pediatrics, Yale University School of Medicine, and the Children's Clinic, Grace-New Haven Community Hospital.

This study was aided by a grant from the Fluid Research Fund of the Yale University School of Medicine.

(Received for publication May 1, 1948.)

The first patient is an example of a relatively uncomplicated case of streptococcal vaginitis.

Case 1: M.M., an eleven-year-old girl was admitted to the New Haven Hospital who two weeks prior to admission had developed a yellow vaginal discharge which was thought at first to be associated with menarche. Four days later the discharge was still present and in addition she had developed a sore throat, temperature elevation, and generalized malaise. One week prior to admission the attending physician obtained a vaginal culture which was positive for hemolytic str. Local antiseptic douches were instituted at home. Because of the patient's failure to respond to this therapy hospitalization was advised. A five-year-old sibling had an upper respiratory infection with a sore throat one week prior to the onset of the patient's illness. Family and past history were otherwise non-contributory.

Physical examination: The temperature was 38° C. on admission. The tonsils had been removed. The anterior pillars were slightly injected. The labia majora were slightly excoriated, and the vaginal orifice was markedly inflamed. A thick yellow discharge exuded from the vagina.

Laboratory data: RBC, 5.2 million; Hgb., 12 gm./100 cc. blood; WBC 14 thousand; urine, essentially normal except for 8-10 white blood cells per low power field; nasopharygneal culture, hemolytic str. group A, type 25; vaginal culture, hemolytic str., group A, type 25; antifibrinolysin, 1-3 hours; Kahn, negative; sulfanilamide blood level, 11.8 mg./100 cc.

Clinical course: The child was placed on sulfanilamide by mouth (1940) for four days. Twenty-four hours after therapy was begun the discharge was completely absent, and the vaginal mucosa was much less inflamed. A vaginal culture after discontinuing medication was negative for hemolytic str. The patient was discharged on the eighth hospital day.

The second case is chosen to illustrate an essentially asymptomatic patient at the time of her first clinic visit. This patient is also of particular interest since a hemolytic str. Group A, type 26, was recovered from the first vaginal culture, and a hemolytic str. Group G was recovered from a vaginal culture 17 months later.

Case 2: G.A., a seven-year-old girl under foster home care, was admitted to the clinic for a routine physical examination, because she was being transferred to another bureau's care. There were no complaints; the child had been well.

Physical examination: The pharynx was slightly injected, and the tonsils were enlarged. There was a soft systolic murmur at the apex of the heart.

Laboratory data: Nasopharyngeal culture, pneumococci; vaginal culture, hemolytic str. group A, type 26; Kahn, negative; urine, essentially normal; Schick, negative.

Clinical Course. Because of the culture report the child was recalled to the clinic for further examination. The vaginal mucosa was markedly reddened, and a scant serous discharge was present. A repeat culture showed pneumococci. Therapy consisted of warm boric acid douches twice daily. Eleven days later there was no excoriation or discharge. When seen in the clinic 17 months later on a routine visit a vaginal culture was positive for hemolytic str., group G. The patient was asymptomatic.

The third case is of unusual interest, for it combines streptococcal pharyngitis, vaginitis, peritonitis, and pelvic abscess.

Case 3: E. F., a 2½-year-old girl was well until 19 days prior to admission when she was vaccinated for smallpox. Ten days later she developed a fever which lasted only one day. When allowed up two days later this child seemed well but walked with a partial stiff-knee gait. The following day, six days before admission, she became irritable and lethargic. She then complained of a sore throat and abdominal pain, refused food, took fluids in limited amounts, vomited occasionally, and slept much of the time. Body temperature was thought to have been elevated occasionally. Family history and past history were irrelevant.

Physical Examination: The admission temperature was 39.6° C. The child appeared acutely and seriously ill. There was a faint pin point macular rash on the back. The color was sallow but not cyanotic. There was some anterior nasal discharge. The tonsils and pharynx were a diffuse bright

red. The anterior cervical nodes were slightly enlarged and tender. The heart rate was rapid, and the tones were of poor quality. There was a soft, blowing, systolic murmur at the apex. The abdomen, which was held rigid, seemed diffusely tender with a suggestion of more tenderness on the left.

Laboratory Data. RBC, 5.4 million; Hgb., 13 gm./100 cc.; WBC, 12.8 thousand; urine, essentially normal except for acetone 4+; nasopharyngeal culture, hemolytic str., Group B; vaginal culture, hemolytic str., Group B; stool culture, hemolytic str.; blood culture, negative; pelvic abscess, drained 12 days after admission, hemolytic str., Group F; chest film, indeterminate.

Clinical Course. The patient received parenteral fluids, sulfadiazine by clysis and by mouth. Body temperature gradually returned to approximately normal, though the white blood cell count continued to rise. It was felt that the child's abdominal symptoms and related physical findings could be explained on the basis of a hemolytic streptococcal peritonitis. The diffuse tenderness and rigidity gradually subsided. On the eleventh hospital day a mass, which was hard, smooth, and about the size of a small grapefruit, was palpated in the left lower quadrant. Associated with these clinical findings there was a temperature elevation to 39.8° C., and a WBC of 32.5 thousand with 81% polynuclear leukocytes. The following day an abscess in the left lower quadrant was drained of about 60 cc. of a milky pus with a fetid odor which was indescribable to the surgeon. Convalescence was rapid thereafter, and the patient was discharged on the eighth post-opeartive day.

Discussion

Twenty-five of the patients with vaginal cultures positive for hemolytic str. were seen on the In-Patient Service; 12 were seen in the Clinic. The presenting complaints and chief symptomatology were referable to the vaginitis in 16 of the patients. Nine of these patients were hospital cases; the other seven were clinic patients. In addition, hemolytic streptococcal vaginitis was seen associated with four cases of scarlet fever and one

TABLE I

Age Distribution of Children with Hemolytic Streptococcal Vaginitis

Age	No. of Cases	Age	No. of Cases	Age	No. of Cases
0–6 mo.	3	4–5 yr.	5	9–10 yr.	1
6 mo.–1 yr.	1	5–6 yr.	3	10–11 yr.	2
1–2 yr.	3	6–7 yr.	4	11–12 yr.	2
2–3 yr.	5	7–8 yr.	1	12–13 yr.	1
3–4 yr.	2	8–9 yr.	3	13–14 yr.	1

each of streptococcal pharyngitis, streptococcal fever, impetigo, erysipelas of the genitalia, streptococcal peritonitis, and streptococcal osteomyelitis.

The vaginal discharge was an acute symptom in the majority of the cases, though at the time of her initial examination, one child gave a history of slight vaginal discharge for several years. A hemolytic str., group A, was recovered from that patient. The parents and the examining physicians described the discharge as thick, thin, creamy, white, green, yellow, and in two histories it was reported as occasionally blood tinged. One of these children with a blood tinged discharge had a foreign body associated with the hemolytic str. In general the discharge was described as slight. It was odorous on several occasions but foul only once. Inflammation of the vaginal mucosa and labia was present to varying degrees. One patient had erysipelas of the perineum.

There was a suggestion of more local inflammation in those children with streptococcal vaginitis and a thicker, more creamy discharge in those children with gonococcal vaginitis. However, it could not be said that the vaginal discharge or physical findings were sufficiently characteristic to be diagnostic with respect to etiology.

Though our cases of hemolytic streptococcal vaginitis were found in all age groups the preponderance of cases occurred in children from one through nine years of age. (Table I)

There was a definite increased incidence of streptococcal vaginitis during the fall and winter months. (Figure 1)

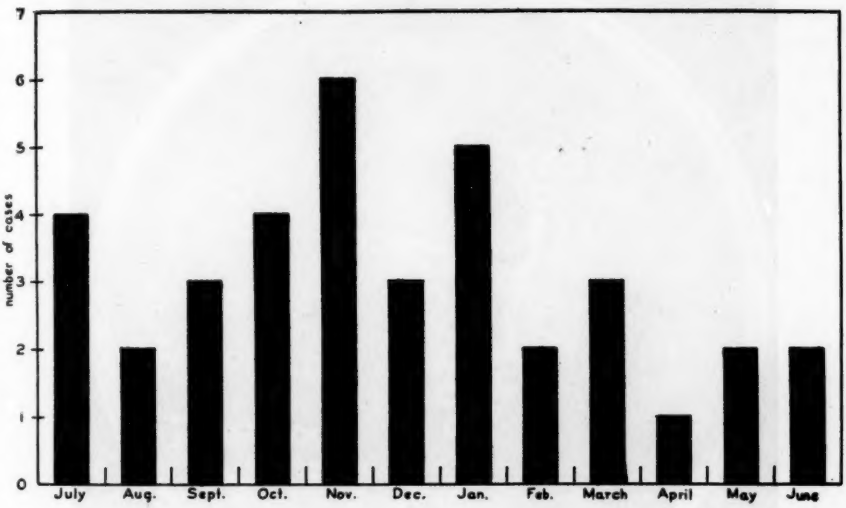


FIG. 1. Seasonal incidence of streptococcal vaginitis.

The hemolytic str. were often recovered from the vagina in pure culture. (Figure 2) In the majority of the cases the streptococci were grouped. Twenty-one were in Group A, four were in Group B, and five in Group G. Of the 30 patients with nasopharyngeal cultures hemolytic str. were present in 17. In 13 instances these organisms were grouped and in every case they were found to be of the same group as those found in the vagina. (Table II)

TABLE II

SUMMARY OF CULTURES

Hemolytic str.	Vaginal	Nasopharyngeal
Group A	21	11
B	4	2
G	5	0
not grouped	7	4
Total	37	17

Eight types; namely, 5, 8, 11, 12, 13, 24, 25, and 26 were represented in 11 of the Group A hemolytic str. recovered from the vagina and typed. One could not be typed. Three types, 11, 13, and 25, were represented in the four Group A hemolytic str. recovered from the nasopharynx and typed. In every case where grouping and typing of the nasopharyngeal and vaginal streptococci were done the organisms were found to be identical.

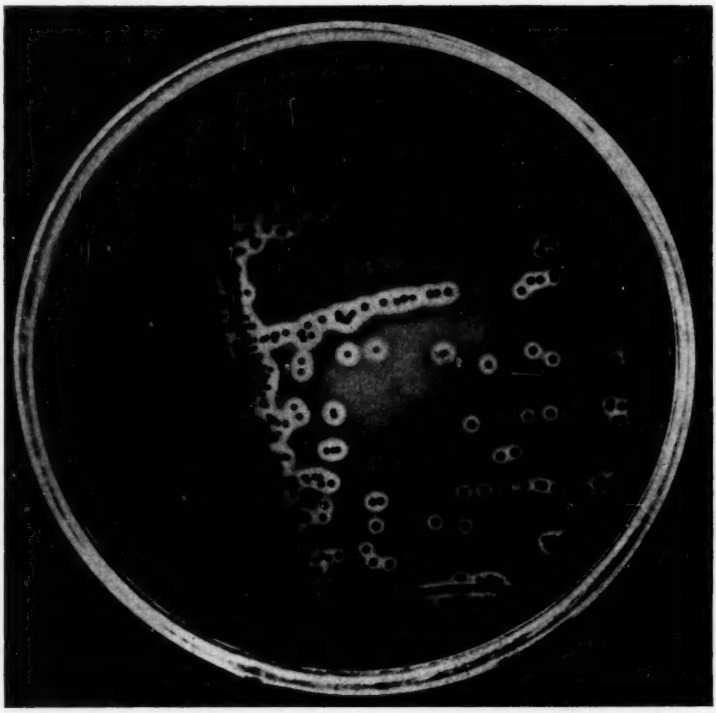


FIG. 2. Hemolytic str. recovered on vaginal culture from a patient with vaginitis.

One of us, P.L.B.,[5] took cultures from the fingers of 60 infants and children who were under treatment for a variety of illnesses in the clinic and wards of the New Haven Hospital. Hemolytic str. were recovered from six and pneumococci from two. This fact can not be overlooked when one is considering the possible modes of entry of the streptococcus into the vagina.

The genital route as a portal of entry in children with primary peritonitis is suggested in the third case report and indicates that a clue into the possible etiology of such cases may be obtained from vaginal cultures.

Treatment of streptococcal vaginitis prior to the advent of the sulfonamides consisted in local therapy such as douches and sponging the external genitalia. With the introduction of the sulfonamides they were used parenterally or locally instilled in capsules as suppositories. The number of cases treated with each drug by the various routes is too

small to allow for generalization beyond saying that equally good results were obtained by either local or parenteral therapy. To our knowledge there have been no recurrences of streptococcal vaginitis in those patients treated with chemotherapy. Two children have now received parenteral penicillin. The results with this form of therapy have been satisfactory, and it is considered the treatment of choice at present.

Summary

The value of culturing all vaginal discharges can not be overemphasized. Hemolytic streptococcal vaginitis has been misdiagnosed as gonococcal vaginitis when only a direct smear of the discharge has been utilized for diagnostic purposes. Hemolytic str. are frequently found in the nasopharynx of those children with hemolytic streptococcal vaginitis. In those instances where grouping and typing of the streptococci from both the vagina and the nasopharynx were done, the same group and the same type were found in both places.

References

1. Hare, R., Haemolytic streptococci from vagina of febrile and afebrile parturient women, J. Path. & Bact. **38**:129, 1934.
2. Weinstein, L., Bacterial flora of human vagina, Yale J. Biol. & Med. **10**:247, 1938.
3. Hardy, Grace C., Vaginal flora in children, Am. J. Dis. Child. **62**:939, 1941.
4. Schaefer, G., Treatment of vaginitis with new synthetic phenol derivative, Quart. Bull., Sea View Hosp. **7**:243, 1942.
5. Boisvert, P. L., and Powers, G. F., Eczema and hemolytic streptococcal disease in children, Yale J. Biol. & Med. **16**:595, 1944.

Spanish Abstract

Vaginitis por Streptococo Hemolitico en las Niñas.

La vaginitis por streptococo hemolitico ha sido erroneamente diagnosticada como vaginitis gonococcica cuando se ha confiado el diagnostico solamente al examen directo de la preparacion.

Este estudio esta basado en cultivos realizados a 286 pacientes vistos en el Servicio de Pediatria de 1925 a 1945 y en la Clinica Pediatrica del 1935 al 1945. Quinientos vienticuatro cultivos vaginales fueron examinados de ellos 37 pacientes (12.9%) con streptococo hemolitico, 33 con gonococo y 11 con neumococo.

Cultivos de la naso faringe fueron hechos en 30 de los 37 pacientes con vaginitis streptococcica. El streptococo hemolitico estuvo presente en 17. En 13 veces estos organismos fueron clasificados y en todos los casos se comprobo que pertenecian al mismo grupo de los que fueron encontrados en la vagina.

Las molestias y sintomas principales de la vaginitis fueron comprobados en 16 de los pacientes. La vaginitis por streptococo hemolitico estuvo asociada en 4 casos a la escarlatina y en una ocasion a la faringitis streptococcica, a la fiebre estreptococcica, al impetigo, a la erisipela de los genitales, a la peritonitis streptococcica y a la ostemielitis streptococcica.

El flujo vaginal fue un sintoma agudo en la mayoria de los casos. El flujo vaginal y los signos fisicos no fueron sin embargo en la mayoria de la ocasiones suficientement caracteristicos para establecer el diagnostico etiologico.

La penicilina por via parenteral es considerada como el tratamiento de eleccion de estos casos en el momento presente.

789 Howard Ave., New Haven
Indiana University Medical Center, Indianapolis

SEVERE ERYTHEMA MULTIFORME OF THE PLURIORIFICIAL TYPE (STEVENS-JOHNSON SYNDROME)

Resulting in Blindness in a Patient Treated with Trimethadione (Tridione)

By BERTRAM SHAFFER, M.D., AND PAUL MORRIS, M.D.
Philadelphia, Pa.

TRIMETHADIONE (Tridione*) is a drug recently introduced for the treatment of petit mal and related disorders.[1, 2] Many toxic effects of the drug have been described. Davidoff's listing[3] included abnormal psychologic behavior, irritability, fatigue, malaise, headache, drowsiness, stupor, status epilepticus, increase in grand mal seizures, variations in the white blood cell count and variations in body temperature. Severe reactions in the form of fatal aplastic anemia (Harrison et al[4]) and also agranulocytosis (Mackay and Gottstein[5]) have also been reported.

Ocular manifestations were quite common. These consisted of a temporary sensitivity of the eyes to bright daylight, blurring of vision and changes in color perception.[1, 3]

Cutaneous effects have been variously described as "skin rashes"[1] and "skin eruptions."[2] More definite entities included scarlatiniform eruption,[3] acneiform skin reaction[3, 6] and exfoliative dermatitis.[3]

The malignant febrile type of erythema multiforme in which the cutaneous manifestations feature purpuric and/or bullous lesions and the orificial mucosae are prominently and severely involved has been described under a number of different names. These included among others, ectodermosis erosiva pluriorificalis,[7] a new eruptive fever associated with stomatitis and ophthalmia (Stevens-Johnson Syndrome),[8] and dermatostomatitis.[9] The largest series of these cases has recently been reported by Costello,[10] who suggested the name "erythema bullosum malignans-pluriorificial" type.

A complete review of the literature dealing with this condition has been compiled by Lever[11] and its essential identity with erythema multiforme exudativum has been stressed by Keil[12] and Lever.[11]

The introduction of a new drug, in spite of the most meticulous laboratory experimentation and clinical evaluation, all too commonly is followed by unfortunate reactions, which are discovered only after extensive clinical trial.

The malignant orificial type of erythema multiforme has never been reported following the use of trimethadione. We have had the opportunity of treating a patient after he had developed this disease while under treatment with trimethadione. Furthermore, the severe involvement of the conjunctivae resulted in total permanent blindness. For these reasons, we believe this case worthy of a report.

CASE REPORT

A. G., a white boy, aged 6½ years, was admitted to the Pediatric Service #2 of the Mt. Sinai Hospital.

From the Dermatologic Service and Pediatric Service #2 of the Mt. Sinai Hospital.
(Received for publication May 11, 1948.)

* Brand name for 3,3,5-trimethyloxazoladine 2-4 dione, a product of the Abbott Laboratories, North Chicago, Ill.

Under a diagnosis of "general retardation of mental development" and petit mal, he had received from his physician six injections of a polyvalent anterior pituitary extract (Polyansin)* between October 8 and October 25, 1946 in doses varying from 0.5 cc. to 1.0 cc. at intervals of two to five days. In addition, trimethadione, in a dosage of 0.3 gm. twice a day was begun on October 10 and continued until October 26.

On October 23, over the site of an injection of pituitary extract given several hours previously, a

FIG. 1. Patient on third day of hospitalization showing extensive hemorrhagic and bullous manifestations. Orificial mucosae are involved but only the fissured, crusted and swollen lips are observable here.

red spot appeared on the left buttock. By the next day this region had become swollen and within 48 hours it was noticed that the lips and eyelids were swollen. On this date (October 25) another injection of extract was administered in the opposite buttock. No local reaction appeared subsequently at this site.

The following day blisters were noted about the lips and it was at this time that trimethadione was discontinued and penicillin totalling 240,000 units over a period of 24 hours was given. By

* A product of the Armour Laboratories, Armour & Co., Chicago, Ill.

October 27, a generalized eruption was apparent, accompanied by fever, a severe cough and dyspnea resembling asthma.

The family history was unimportant except that the only sibling, a boy aged four years, had been born with bilateral dislocation of the hips.

The patient's birth was normal. He had walked at 1½ years and talked at 2½ years. He had escaped the exanthematous diseases of childhood.

Examination on admission revealed an acutely ill child who presented a generalized florid eruption of multiform character. Most of the lesions were red to violaceous, blotchy macules and papules. Many of these were purpuric. Bullae were present over the knees, thighs, chest and neck. Some of the blebs arose from apparently normal skin while others had developed obviously from preexisting maculo-papular lesions. They were distended with either clear or hemorrhagic fluid. The palms and soles were diffusely mottled and swollen.

The lips were fissured, bleeding and covered with blebs, erosions and exudate. The tongue was diffusely coated and enlarged. The whole interior of the mouth including the buccal mucosa, the gingivae, the tonsillar areas, the palate, and the pharynx, presented a confluent mass of swollen, boggy pseudomembranous formation. The eyelids were adherent to each other. They were separated with great difficulty and revealed the presence of a profuse purulent discharge. The genitals were swollen and the glans penis was completely encased in a bullous lesion which later ruptured, leaving a denuded glans.

In the chest, wheezing, expiratory rales were heard anteriorly and large rhonchi were detected posteriorly. The systemic physical examination was otherwise normal. The pulse was 140, the respiratory rate 30, and the rectal temperature 40° C.

For a period of one week the cutaneous manifestations became more severe. In particular, the hemorrhagic phenomena become more pronounced. The disease took on the character, eventually, of a pure bullous and purpuric eruption. At the end of this period the cutaneous picture began to subside and following another week of declining activity new skin lesions stopped appearing. The severe character of the eruption on the mucosae continued, however. Although the mouth lesions began to subside shortly following those on the skin, the glans penis remained the site of a weeping erosion until November 25.

It was on the conjunctivae that the disease was most persistent and destructive. The ophthalmologic consultant, Dr. I. S. Tassman, examined the child's eyes on November 5 and stated that "both upper lids on eversion show a rather thick membrane covering the tarsal surface. The membrane is adherent ——." "The corneae of both eyes are clear." Four days later he noted that the left cornea was the site of a ruptured bleb and abscess formation. Within 48 hours the right eye became similarly involved, and by November 13 the lens of this eye had herniated through the perforated cornea. The corneal ulcerations healed by November 28 with the formation eventually of flattened white opacities, resulting in complete blindness. The right upper lid became attached to the eyeball.

During the first two weeks' stay in the hospital the boy's condition was critical. His chance of recovery seemed very uncertain. The cough and wheezing respirations became very severe, and the fever remained high. Feeding was carried out by introducing nourishing liquids through a stomach tube introduced through the nostril and allowed to remain in place. The temperature dropped slowly from a peak of 40.6° C. to 37.8° C. Later it gradually became normal. The blood count on October 28 was Hgb. 11.4 gm./100 cc. blood, WBC 16.9 thousand, polynuclear neutrophiles 69%, non-segmented neutrophiles 18%, and lymphocytes 13%. Several urine examinations showed the presence of occasional white blood cells, and at times a few red blood cells. Blood cultures taken on three occasions were negative. The prothrombin time was 100%. The total protein estimation of the blood was 5.7 gm./100 cc. The blood urea nitrogen was 9 mg./100 cc. Cultures of the eyes revealed hemolytic Staph. aureus. A roentgenogram of the chest on November 5 showed small areas of pneumonitis in the left upper lobe and right lower lobe.

The patient's systemic treatment consisted of intramuscular injections of penicillin and streptomycin, fluids by mouth, saline and glucose solution intravenously, and plasma intravenously.

The eyes were treated by means of frequent boric acid lavage and the local instillations of atropine 1% and penicillin solution.

An attempt was made to prove the drug etiology of this disease by passive transfer tests, using the Prausnitz-Küstner technic with blood serum, as well as by the Urbach-Koenigstein technic using

blister fluid.[13] In addition, patch tests were applied over the sites where either serum or blister fluid had been injected previously in a normal subject (P.M.) according to a technic formerly described.[14]

The suspected allergens injected were trimethadione 0.2% aq. suspension and pituitary extract 25% aq. sol. The patch test material consisted of 25% concentration of each of the above preparations in cholesterinized petrolatum. All these tests proved to be negative.

The injection of the patient's serum 0.1 cc. intradermally into a normal subject (B.S.), followed 24 hours later by the ingestion of 0.3 gm. of trimethadione, failed to produce a positive reaction.

Fluid drawn from an early bulla was tested for the presence of virus at the Virus Laboratory of the Children's Hospital,* with negative results.

Discussions

That drugs give rise to bullous eruptions of the type herein described is well established by numerous reports. These include many commonly used drugs such as the barbiturates,[15] and sulfonamides,[16] bismuth,[17] iodides,[18] and phenytoin sodium.[19] It is unfortunate that in the case of most drug eruptions no satisfactory test exists for proving the role of the inciting agent. It is only in exceptional instances that objective tests have given positive results.[14]

It is not surprising, therefore, that we failed to substantiate our suspicions in this case even after performing a rather large battery of allergy tests. To prove this diagnosis by the readministration of the suspected drug to the patient, in view of the already disastrous results, could hardly be countenanced.

In spite of the fact that anterior pituitary extract has been used extensively for many years, we could find no report of a skin reaction attributed to its use.

On the other hand, skin eruptions, as well as numerous other toxic effects, are already recognized as part of the known actions of trimethadione, after only a rather limited clinical experience. Therefore, if one is to attribute the etiology of the eruption herein described to a drug, it would seem logical to assign trimethadione the responsible role rather than pituitary extract.

The fact that the eruption appeared originally at the site of a preceding injection of anterior pituitary extract may be a coincidence, or it may be due to a non-specific traumatic localizing effect (Koebner reaction). It will be recalled that, when a subsequent injection of anterior pituitary extract was given in the opposite buttock, the reaction was not repeated. This would seem to indicate the incidental nature of this observation.

Conclusions

A case of severe erythema multiforme of the pluriorificial type resulted in total complete blindness due to bilateral involvement of the cornea.

This eruption followed the administration of trimethadione and anterior pituitary extract. The possibility that trimethadione was the cause of the syndrome was considered.

References

1. Lennox, W. G., Petit mal epilepsies—their treatment with tridione, J.A.M.A. **129**:1069, 1945.
2. DeJong, R. N., Effect of tridione in control of psychomotor attacks, J.A.M.A. **130**:565, 1946.
3. Davidoff, E., Tridione therapy in institutionalized patients, New York State J. Med. **47**:1492, 1947.
4. Harrison, F. F., Johnson, R. D., and Ayer, D., Fatal aplastic anemia following use of tridione and hydantoin, J.A.M.A., **132**:11, 1946.

* Through the courtesy of Dr. Joseph Stokes, Jr., Director of the Children's Hospital, Philadelphia, who saw this patient in consultation and who agreed with the diagnosis of probable trimethadione reaction.

5. Mackay, R. P., and Gottstein, W. K., Aplastic anemia and agranulocytosis following tridione, J.A.M.A. **132**:13, 1946.
6. Shaffer, B., Personal observation.
7. Rendu, R. M., Sur un syndrome caractérisé par l'inflammation simultanée de toutes les muqueuses externes—, Rev. gén. de clin. et de therap. **30**:351, 1916.
8. Stevens, A. M., and Johnson, F. C., New eruptive fever associated with stomatitis and ophthalmia, Am. J. Dis. Child. **24**:526, 1922.
9. Baader, E., Dermatostomatitis, Arch. of Derm. and Syph. **149**:261, 1925.
10. Costello, M. J., Erythema multiforme exudativum (erythema bullosum malignans-pluriorificial type), J. Investigative Dermat. **8**:127, 1947.
11. Lever, W. F., Severe erythema; two cases of type ectodermosis erosiva pluriorificialis with development of cicatricial conjunctivitis and keratitis in one case, Arch. Dermat. & Syph. **49**:47, 1944.
12. Keil, H., Erythema exudativum (Hebra); clinical entity associated with systemic features, Ann. Int. Med. **14**:449, 1940.
13. Urbach, E., and Gotlieb, P. M., Allergy, 2nd Ed., Greene and Stratton, New York, 1946, p. 150.
14. Shaffer, B., Lentz, J. W., and McGuire, J. A., Sulfathiazole eruptions. Sensitivity induced by local therapy and elicited by oral medication, J.A.M.A. **123**:17, 1943.
15. Berlin, C., Ectodermosis erosiva pluriorificialis due to phenobarbital; Acta Medica Orientalis **6**:67, 1947.
16. Greenberg, S. I., and Messer, A. L., Fatal bullous dermatitis following administration of sulfadiazine, J.A.M.A. **122**:944, 1943.
17. Shaffer, B., and Collins, L. H., Jr., Pemphigoid eruption associated with hemorrhagic nephritis following bismuth therapy, Arch. Dermat. & Syph. **45**:57, 1940.
18. Ormsby, O. S., Diseases of the Skin, 4th Ed., Lea and Febiger, Philadelphia, 1934, pp. 184-186.
19. Ellis, F. A., Reactions to nirvanol, phenytoin sodium, and phenobarbital, South. M. J. **36**:575, 1943.

SPANISH ABSTRACT

Eritema Grave Multiforme de Tipo Pluriorificial. (Sindrome de Stevens-Johnson)

Un caso de eritema grave multiforme buloso del que resulto completa ceguera debida a la affeccion bilateral de las corneas es describido.

La erupcion seguida de la administracion de trimetanione (tridione) y polyansin (extracto pituitario anterior). El uso del extracto pituitario anterior despues de muchos años de uso no habia sido nunca reportado como causa de erupcion. La tridione despues de un uso limitado en la clinica es ya reconocida como la causa de muchas reacciones incluyendo las de la piel. Por consiguiente la posibilidad de señalar la tridione como causa de esta erupcion es seriamente considerada.

1825 Pine St.

CLINICAL USE OF ALCOHOL-REFINED TOXOIDS

By J. M. RUEGSEGGER, M.D., AND G. K. LOOSER, M.D.
Pearl River and Nyack, N.Y.

THE role of toxoids of diphtheria and tetanus in artificial immunization is well established in this country and other areas influenced by Western medicine. Observations made during World War II among members of the American armed forces reemphasized the value of these toxoids. If further evidence of the efficacy of tetanus toxoid were required, the extremely low incidence of tetanus among members of the American and British armed forces in recent years would be decisive. During the retreat from Dunkirk, no cases of tetanus were seen among British soldiers protected with toxoid. There were only six known cases of tetanus among more than 10,000,000 soldiers of the United States Army whose immunization records showed a full complement of basic inoculations.[2] Similarly, only two cases of tetanus were seen among United States Navy personnel who had received at least two injections of alum-precipitated tetanus toxoid prior to the injury.[3] On the other hand, neither the Army nor the Navy included diphtheria toxoid among routine immunization procedures; several observations among these personnel disclosed an alarming incidence of susceptibility to diphtheria.[4,5] A similar observation has been made among civilian groups[6,7] and will undoubtedly deserve further consideration as a public health measure.

Since the introduction of diphtheria toxoid by Ramon, several modifications have been made which tended to increase the popular and general use of that toxoid and subsequently of tetanus toxoid. These modifications have usually been directed toward increasing the antigenicity of the toxoid and toward diminishing the number of reactions after parenteral administration. The incidence of general and severe local reactions among adults has discouraged popular public health programs, involving the use of diphtheria and tetanus toxoids, among older age groups. The use of simplified and synthetic media for production of tetanus toxin[8] represents a distinct improvement because of the elimination of many of the sensitizing proteins of the broth media. Recently, Pillemer and his colleagues[9,10] described a new method of refining toxins and toxoids which marks another milestone in the method of producing toxoids for human use. The commercial application of this method of refining diphtheria and tetanus toxoids should make mass immunization feasible now; whereas, formerly the incidence of reactions among adults constituted a hazard not easily overcome.

Briefly, this method consists of the refinement of toxoids from the parent cultures by precipitation with methanol under rigidly controlled conditions of ionic strength, pH, temperature and protein concentration. The end-product of these procedures is a purified toxoid powder which contains 0.3% of the nitrogen contained in the original culture filtrates; the refinement, thus, eliminates approximately 99.7% of nitrogen. Hence, in theory at least, it is possible to reduce the size of a dose to one three hundredth that of former toxoids. However, a volume of 0.5 Ml. will probably be used generally for the sake of convenience of injection and of standardization of toxoid dosage. Preliminary tests in small animals showed that these alcohol-refined toxoids were at least as antigenic as unrefined toxoids in an equivalent Lf dosage. Likewise, these toxoids passed the tests for safety and antigenicity prescribed by the National Institute of Health for

(Received for publication April 19, 1948.)

toxoids for human inoculation. The high degree of concentration of toxoid eliminates the necessity for alum as a concentrating agent; its use exclusively as an adjuvant with alcohol-refined toxoids permits its concentration to be reduced to 5 mg./100 cc. or less, per dose. Thus the physical and biologic properties of these toxoids seemed ideal for the human clinical trials described below.

Thirty-one adults were selected for the first series of observations for reaction to the toxoids of diphtheria and tetanus. These people presented a variable history concerning previous immunization to diphtheria and tetanus. Approximately half of the group recalled a childhood series of inoculations for the prevention of diphtheria, but only one subject had had such a series within the preceding five years. Neither Schick nor Moloney tests were performed; it is interesting to record that there was little correlation between the pre-inoculation diphtheria antitoxin titrations of the blood sera and the history of previous prophylaxis. Twenty-seven of the group gave a reliable history of previous immunization against tetanus; preliminary antitoxin titrations beforé inoculation tended to confirm the negative history in the remaining four.

Twenty-four of this group received the alcohol-refined toxoids of diphtheria and tetanus. The remaining seven asked to be excused from diphtheria inoculations because of a previous severe reaction following the inoculation of ordinary diphtheria toxoid; these latter subjects received only alcohol-refined tetanus toxoid. Each subject received two intramuscular injections of toxoid in the upper arm at intervals of five weeks. The alum-precipitated forms of the toxoids were employed and concentrations of 20 Lf diphtheria toxoid and 12 Lf tetanus toxoid in doses of 0.3 Ml. were used throughout. Subjects were observed for local reactions and questioned concerning constitutional reactions. None experienced constitutional symptoms, but accurate observations concerning body temperature were not made. Erythema at the site of injection was noticeable in most of this group within 24 hours of the injection but significant local reactions were observed in only five of the subjects following the first inoculation; these reactions consisted of maximal erythema with or without pain. Three of these subjects had sufficient associated edema to cause awareness of pain on motion but none was prevented thereby from the normal exercise of daily duties; lymph node enlargement was not an associated finding in any of these subjects. In all, the local reaction began to wane within 48 hours and had disappeared within 96 hours. Reactions were fewer and distinctly less intense, even among the original five described above, following the second injection five weeks later. No evidence of residual induration or tenderness could be observed by palpation one month after each inoculation.

Titrations of antitoxin of the subjects' sera are shown in Table I; the numbers marked with an asterisk denote those subjects who received only tetanus toxoid. If a titer of 0.004 unit be considered the smallest amount of circulating antitoxin compatible with a negative Schick test, it may be presumed that almost half of the group would have shown a positive Schick test originally;[11] similarly the same number might have been considered to be susceptible to diphtheria.[12] Yet two months after the first inoculation, all of the group who received the combined toxoids had titers well in excess of that considered necessary to protect against diphtheria; in passing, it might be mentioned that the increase in diphtheria antitoxin titer of five of the subjects who received only tetanus toxoid may be presumed to be anamnestic in origin. Of the 24 subjects receiving the combined toxoids, only two showed titers at the end of one year which were not compatible

with resistance to diphtheria; these two subjects showed 30- and 250-fold increases respectively after two months, but began to show distinct decreases at the time of the six months titrations.

There was no individual correlation between diphtheria antitoxin titers and tetanus antitoxin titrations. Although the value of tetanus toxoid is undisputed, there has not yet been published a precise correlation between serum antitoxin titers and susceptibility to tetanus. It has been estimated by several investigators that serum titers of 0.01 to 0.1 unit may be protective. It may be seen from Table I that 100% of the subjects in this

TABLE I

Number	Diphtheria				Tetanus			
	Before	2 months later	6 months later	1 year later	Before	2 months later	6 months later	1 year later
1	0.02	0.5	0.5–1.0	0.2–0.5	0.02	2–3	1–2	1
2	0.002	0.02	0.1–0.4	0.01	trace	2	1–2	1
3	1.0	12	6.0–12.0	16	0.5–1.0	3–5	1–2	1
4*	0.04–0.1	0.2	0.2	0.2	0	0.2–0.5	0.2–0.5	0.01–0.1
5*	0.004	0.02	0.01–0.02	0.01	0.2	25	5	4
6	0.004	0.2	0.5	0.2–0.5	0.2	35–40	12	4
7	0.001	0.02	0.1–0.4	0.04	0.04–0.1	15–20	3	3
8*	0.2	2.0	0.2–0.5	0.2	0.04–0.1	5–7	2–3	1–3
9	2–4	25	8–16	8–16	0	0.5	0.2	0.01–0.1
10	<0.0005	0.02–0.04	0.01	0.01	0.02	7–9	2	1
11	0.2	2.0	1.0	0.5	1.0	2–4	2	2
12*	<0.0005	0.02	0.0005	0.001	0.04–0.1	9–12	3–5	1–2
13	<0.0005	0.2	0.1	0.02	0.02–0.04	20	2–4	1–2
14	2	40	50	40	2–4	12–15	3–5	3–5
15*	<0.0005	0.0005	0.004	0.0005	1–2	10	5	3
16*	<0.0005	0.002	0.001	0.0005	1–2	8–12	5	3–5
17	0.5	25	20–25	10	0.02	9	3–5	2
18	0.5	8	—	8	0.5–1.0	20–40	—	20
19	<0.0005	0.01–0.02	0.004	0.002–0.004	0	0.2–0.5	0.2	0.1–1.0
20	<0.0005	0.04–0.1	0.02	0.01	1–2	10	5	3
21	0.2	20	25	15–20	trace	15–20	5	5
22*	<0.0005	0.004	0.005	0.0005	0.04–0.1	0.5	1–2	0.1–1.0
23	4.0	30	—	20–25	0.02–0.04	7–9	—	3
24	<0.0005	3.0	0.1	0.02	0.5–1.0	15–20	5	2
25	0.02	1.0	—	0.5–1.0	0.2 –0.5	20–25	—	7
26	0.002	0.01–0.04	0.004	0.02	0.04–0.1	2–3	2	1
27	<0.0005	0.2	0.2	0.04–0.1	6.0	15–20	9	5–7
28	0.01	10–15	15	5–10	1–2	25	7	3–5
29	0.002	0.5	0.01–0.02	0.0005	0.04–0.1	15–20	5	2–3
30	15	25	25–30	35	0	3	0.5–1.0	0.1–0.5
31	0.2	200	100	50	0	0.2–0.5	0.1–0.2	0.01–0.1

* Received only tetanus toxoid.

study possessed such "minimal protective" titers even one year after inoculation; the three who reverted to this minimal range belonged to that group for whom this constituted the first tetanus immunizing course; it may be presumed that so-called "booster" doses will stimulate titers of antitoxin well within a safe range.

The second group of clinical trials was composed of 550 children ranging from 3 to 15 years of age. All had resided at one time in New York City and consequently may be presumed to have had some type of diphtheria immunization. None was known to have received a course of tetanus immunization. All were attending a boarding school about 25 miles from the city for the year during which the observations were made.

TABLE II

Number	Diphtheria				Tetanus			
	Before	2 months later	6 months later	1 year later	Before	2 months later	6 months later	1 year later
1	0.5	32	8	8	0	0.1–1.0	0.1–1.0	0.1–1.0
2	0.001–0.01	8	1	—	0	0.1–1.0	0.1–1.0	—
3	0.1	8	—	—	0	1.0	—	—
4	0.2	16	4	4	0	1.0–2.0	0.2–0.5	0.1–1.0
5	0.5	16	4–8	8	0	2.0–4.0	0.5	0.1–1.0
6	0.1–0.2	2	1	1	0	0.1–1.0	0.1–1.0	0.1–1.0
7	0.004–0.01	4–8	0.5–1.0	—	0	1.0–2.0	0.2–0.5	—
8	0.2	—	—	—	0	—	—	—
9	2.0	12	4	8	0	1.0–2.0	0.5–1.0	0.1–1.0
10	2.0	24	4–8	8	0	1.0–2.0	0.5–1.0	0.1–1.0
11	0.02–0.04	4	2	2–4	0	0.1–1.0	0.01–0.1	0.1–1.0
12	0.5	32	8	4	0	0.1–1.0	0.1–1.0	0.1–1.0
13	4.0	80–160	16–32	8–16	0	2.0–4.0	0.5–1.0	0.1–1.0
14	0.5	100	16–32	—	0	1.0–2.0	0.5–1.0	—
15	1.0	64	8	8	0	0.1–1.0	0.1–1.0	0.1–1.0
16	1.0	16	4	2–4	0	0.1–1.0	0.1–1.0	0.1–1.0
17	1.0	32	8	—	0	2.0	0.5–1.0	—
18	0.5	32	4–8	4–8	0	0.1–1.0	0.1–1.0	0.1–1.0
19	0.2	32	8	—	0	0.1–1.0	0.1–1.0	—
20	0.5	100–150	32	—	0	0.1–1.0	0.1–1.0	—
21	0.1	4	1	—	0	1.0–2.0	0.5–1.0	—
22	0.1	8	4	—	0	1.0–2.0	0.2–0.5	—
23	0.1	48	1	0.5	0	1.0	0.2–0.5	0.1–1.0
24	0.2	8–16	2	0.5–1.0	0	—	0.1–1.0	0.1–1.0
25	0.04	2	1	0.5	0	—	0.1–1.0	0.1–1.0
26	0.5	8–16	—	—	0	0.1–1.0	—	—
27	0.1	1–2	0.2–0.5	1.0	0	0.1–1.0	0.1–1.0	0.1–1.0
28	0.2	4	4	0.5–1.0	0	0.1–1.0	0.1–1.0	0.1–1.0
29	0.5	8	4	0.5–1.0	0	0.1–1.0	0.1–1.0	0.1–1.0
30	2.0	24	16–32	8–16	0	1.0	0.5–1.0	0.1–1.0
31	0.01	0.5	0.1–0.4	0.04	0	0.1–1.0	0.1–1.0	1–2
32	2.0	—	—	—	—	—	—	—
33	0.5	8	4	—	0	0.1–1.0	0.1–1.0	—
34	2.0	12	2	4	0	0.1–1.0	0.1–1.0	0.1–1.0
35	2.0	12–24	4	2–4	0	0.1–1.0	0.1–1.0	0.1
36	1.0	64–128	16	16	0	1.0	0.1–0.2	0.1
37	0.04	4	1	—	0	0.1–1.0	0.1–1.0	—
38	0.02	2	0.5–1.0	—	0	0.1–1.0	0.1–1.0	—
39	0.5	8	2–4	2–4	0	0.1–1.0	0.1–1.0	0.1–1.0
40	0.5	2	1–2	—	0	0.1–1.0	0.1–1.0	—
41	—	8	2	—	0	0.1–1.0	0.1–1.0	—
42	0.5	8	2	—	0	0.1–1.0	0.1–1.0	—
43	0.5	32	4	—	0	2.0–4.0	0.2–0.5	—
44	1.0	32	4	2–4	0	1.0	0.2–0.5	0.1–1.0
45	0.2	4	2	—	0	1.0–2.0	0.2–0.5	—
46	0.5	16	1–2	2	0	1.0–2.0	0.2–0.5	0.1–1.0
47	0.5	8–16	2–4	2–4	0	1.0–2.0	0.5–1.0	0.1–1.0
48	4.0	10	2	—	0	1.0–2.0	0.2–0.5	—
49	0.04–0.1	1–2	0.1	—	0	0.1–1.0	1	—
50	1.0	32	4	4	0	0.1–1.0	0.1–1.0	0.1–1.0
51	—	—	—	0.002–0.004	—	—	—	0.1–1.0
52	—	—	—	0.002–0.004	—	—	—	0.1–1.0
53	—	—	—	4	—	—	—	0.1–1.0
54	—	—	—	0.02	—	—	—	0.1–1.0
55	—	—	—	2	—	—	—	0.1–1.0
56	—	—	—	4	—	—	—	0.1–1.0
57	—	—	—	4	—	—	—	0.1–1.0
58	—	—	—	2–4	—	—	—	0.1–1.0
59	—	—	—	16	—	—	—	2–4
60	—	—	—	4	—	—	—	0.1–1.0
61	—	—	—	0.2–0.5	—	—	—	0.1–1.0
62	—	—	—	4	—	—	—	0.1–1.0
63	—	—	—	2	—	—	—	0.1–1.0
64	—	—	—	2	—	—	—	0.1–1.0
65	—	—	—	2	—	—	—	0.1–1.0
66	—	—	—	1–2	—	—	—	0.1–1.0
67	—	—	—	16	—	—	—	0.1–1.0
68	—	—	—	1	—	—	—	0.1–1.0
69	—	—	—	0.5–1.0	—	—	—	0.1–1.0
70	—	—	—	2	—	—	—	0.1–1.0
71	—	—	—	2	—	—	—	0.1–1.0

Two inoculations of 0.3 Ml. dose of the combined toxoids in the same concentration as that previously used were given intramuscularly in the upper arm at intervals of five weeks. Again frequent observations were made by the authors and attending staff for reactions to these inoculations. No chills or chilly sensations were observed or complained of by any of the children. Oral temperatures were recorded on every child who reported to the dispensary within 48 hours for whatever reason. Eleven children were thus seen

who had elevations of 37.6° to 38.1°C. but the attending nurse was unable to correlate the fever with the inoculation; and the following day fever was not present when these patients were examined by the physician. Reactions of erythema and local heat were observed in fewer than 10% of the children. Pain was an insignificant feature and no child was prevented from engaging in usual school activities by the post-inoculation reactions. Local reactions appeared within 24 hours and reached their maximum intensity within 48 hours of the injection. Reactions were insignificant following the second injection five weeks later. Here, as in the adult group, no sterile abscesses were produced and even a subcutaneous nodule could not be palpated one month after the inoculation. Titrations of circulating antitoxin were made from approximately 10% of the children. Fifty of the older children, aged 12 to 15, were chosen at random from the older age groups to facilitate the collection of adequate specimens of blood serum. At the end of one year, losses due to discharge, graduation, etc. were compensated for by the addition of 21 other children of the original group in order to assure a sufficient number in the group for continuing studies. These titrations are listed in Table II. All of this group showed evidence of basic immunity to diphtheria and probably none would have responded positively to the Schick test. The increase in antitoxin titer was adequate within two months in all cases and prodigious in extent in many.

There was considerably less variation among tetanus antitoxin titers than among diphtheria antitoxin titers and similarly less variation among the children than among the adults of the first group. The negative history of a previous tetanus immunization was confirmed by failure to find any circulating antitoxin in all of the 50 children tested. Yet within two months after the first inoculation all exhibited an antitoxin titer at least ten times that considered to be a "minimal protective" level. And even after one year, such high levels were maintained.

Discussion

The ideal immunizing agent will be one which produces a minimum of untoward reactions and confers adequate and durable protection. The human immunogenic mechanism may place certain limitations to the attainment of that ideal. But insofar as the evolution of diphtheria and tetanus toxoids has been concerned during the past 25 years, progress has been made toward that goal. Theoretically, the reduction of non-toxoid nitrogen-containing substances of the parent culture should be a factor in the diminution of untoward reactions. In this study, reactions among adults were neither serious nor numerous. While control studies are needed to be decisive, the authors could not escape the impression that many fewer reactions were observed following the 1100-odd inoculations than might have been observed with ordinary toxoids in a group of people previously immunized with the toxoids of diphtheria and/or tetanus. Comparison of these experiences with the reported results of others tends to confirm this impression. Thus, in one series of 240 children of a similar age range,[13] the inoculation of 0.5 Ml. of alum-precipitated toxoid caused reactions in 61%. In our series, no general reactions were seen and local reactions were observed in less than 10% of the group; yet, two factors were operative which might have been expected to increase the likelihood of reactions: (1) the children were from an urban community, living together, and (2) multiple antigens, diphtheria and tetanus toxoids, were inoculated. The great incidence of "toxoid-reactors" among adults[14] has discouraged the institution of broad immuniza-

tion programs among the older age groups of the population.[15] Hence, we are further encouraged to believe that the incidence of five moderate local reactions among 24 adults, many of whom had been previously immunized or intimately exposed to diphtheria toxoid in its preparation, is further evidence of the purity of this type of toxoid.

The adequacy and durability of protection conferred by these toxoids must await further observations for a conclusive evaluation. During the 18 months since the first inoculations of these toxoids, no cases of diphtheria or tetanus have been observed among the subjects of the study. The relative durability of immunity may be gauged by comparing antitoxin titers with other series; such comparisons are subject, of course, to considerable error because of the variation in immunologic factors not capable of precise evaluation. A recent study[16] among Royal Canadian Air Force personnel disclosed that approximately 20% of those adults who were originally Schick-positive became Schick-positive again within 6 to 12 months after receiving two doses of alum-precipitated diphtheria toxoid; and almost one third of the same group reverted to the Schick-positive state within 1 to 2 years of receiving the toxoid. It would thus appear that the routine employment of the Schick test at frequent intervals might be a necessary part of every large immunization program if a majority of the adult population is to be maintained in a non-susceptible state. In our series, approximately 8% of the adults might have been Schick-positive one year after the first of a series of two inoculations of diphtheria toxoid. Among the children, the record was even better for only 4% exhibited antitoxin titers compatible with a positive-Schick reaction one year later. While the two series are different in several immunologic factors which cannot be evaluated precisely, the series of Volk and Bunney[13] may be used as an approximation of antitoxin titers to be expected in reimmunized children. All of the titrations in both groups showed at least 0.001 unit of diphtheria antitoxin after one year; 93% of the Michigan series[13] and 96% of the children of the present series showed titers of at least 0.01 unit; the respective figures for 0.1 unit were 60% and 92%. And 80% of the present series showed at least 1.0 unit/Ml. of circulating diphtheria antitoxin one year after the first inoculation.

The durability of tetanus immunity is more difficult to determine because of our lack of knowledge correlating this information with clinical experience. In this study, every subject, regardless of age or previous immunization to tetanus, responded within two months after the first inoculation with titers in the range of 0.1-1.0 unit of tetanus antitoxin. Moreover, one year after the first inoculation, 96% of the bloods titrated exhibited values within this range; the remaining 4%, showing levels of 0.01-0.1 unit, the presumed minimal protective level, were found among adults for whom this was the first course of tetanus immunization. Again, if series of immunologic studies of different observers may be compared, it can be inferred that the alcohol-refined tetanus toxoid used in this series confers as good, if not better, and a more durable immunity than the tetanus toxoids used previously. For instance, Gold[17] noted that 64.5% of adults showed levels of 0.1 unit six months after the second dose of tetanus toxoid; in the present series, 100% of adults exhibited titers in excess of that level and 90% of adults maintained such levels of tetanus antitoxin even after one year. In a similar comparison with the report of McBryde and Poston,[18] the alcohol-refined tetanus toxoid appears to be a superior antigen. In the former series, 42% of the children had titers of tetanus antitoxin in excess of 1 unit and 58% in the range of 0.1 to 1.0 unit approximately two months after the second injection; corresponding figures in this series are 54% and 46%.

More strikingly, all of the children in the present series showed levels of 0.1 to 1.0 unit after one year; whereas, 10% of the children in the former study showed titers of less than 0.1 unit one year after the second inoculation.

Summary

Alcohol-refined toxoids of diphtheria and tetanus were inoculated into 31 adults and 550 children.

These alum-precipitated toxoids are associated with many fewer and less severe reactions, both in adults and children, than those following the use of ordinary toxoids.

Within the limits of a year's observation after inoculation, such toxoids appear to be able to stimulate an adequate and durable immunity as adjudged by serial antitoxin titrations.

Acknowledgement

The authors wish to express their thanks to the members of the Testing Department of the Lederle Laboratories Division, American Cyanamid Company, for making the antitoxin titrations reported in this manuscript.

References

1. Bensted, H. J., Modern practice in war-time—immunization of soldiers and civilians; immunization against bacterial toxins (Harben lecture), J. Roy Inst. Pub. Health Hyg. **4**:17, 1941.
2. Long, A. P., and Sartwell, P. E., Tetanus in United States Army in world war II, Bull. U. S. Army M. Dept. **7**:371, 1947.
3. Hall, H. W., U. S. Navy's war record with tetanus toxoid, Annals of Int. Med. **28**:298, 1948.
4. Karelitz, S., and Moloshok, R. E., Immunity to diphtheria in Army personnel, War Med. **6**:232, 1944.
5. Young, D. C., and others, Diphtheria outbreak at large naval training center, U. S. Nav. M. Bull. **45**:669, 1945.
6. Levy, A. J., Susceptibility of adult population to diphtheria, Illinois M. J. **82**:390, 1942.
7. Goldsworthy, N. E., and Wilson, H., Schick test in young adults, M. J. Australia **2**:349, 1943.
8. Mueller, J. H. (Boston), Schoenbach, E. B. Jezukawicz, J. J., and Miller, P. A., Production of tetanus toxin on peptone-free media, J. Clin. Investigation **22**:315, 1943.
9. Pillemer, L., Wittler, R., and Grossberg, D. B., Isolation and crystallization of tetanal toxin, Science **103**:615, 1946.
10. Pillemer, L., and Toll, D., Purification of diphtherial toxoid, Science **105**:102, 1947.
11. Brandon, K. F., and Fraser, D. T., Observations on interpretation of Schick tests; comparison of Schick test interpretations using different products on same individuals simultaneously, J. Immunol. **31**:387, 1936.
12. Kane, L. W., Medical progress; skin tests in bacterial and viral diseases, New England J. Med. **232**:728, 1945.
13. Volk, V. K., and Bunney, W. E., Reimmunization against diphtheria of previously immunized children, Am. J. Pub. Health **32**:700, 1942.
14. Hayman, C. R., Reactions following use of diphtheria toxoid; analysis of reactions and of guides to their occurrence, Am. J. Dis. Child. **56**:723, 1938.
15. Bunch, C. P., Morrow, R. C., Jr., Timmons, J. R., and Smith, D. T., Studies on immunization of adults with diphtheria toxoid, J. Immunol. **39**:427, 1940.
16. Sellers, A. H., Baillie, J. H., Cruikshank, J. M., and McKibbon, J. C., Findings on re-Schick testing of air force personnel, Canad. J. Pub. Health **36**:390, 1945.
17. Gold, H., (Chester, Pa.) Studies on tetanus toxoid; active immunization of normal persons with tetanus toxoid, alum-precipitated, refined, J.A.M.A. **109**:481, 1937.

18. McBryde, A., and Poston, M. A., Immunization with tetanus toxoid; persistance of antitoxin and effect of stimulating doses of alum-precipitated tetanus toxoid after five-year period, J. Pediat. **28**:692, 1946.

SPANISH ABSTRACT

Uso Clinico de los Toxoides Refinados con Alcohol

Toxoides de difteria y tetano fueron refinados por precipitacion con metanol bajo un rigido control de su concentracion ionica, pH, temperatura y concentracion proteinica. Este metodo de refinacion resulta de la eliminacion del 99.7% del nitrogeno de los cultivos filtrados. Los toxoides combinados difteria y tetano fueron inoculados en 31 adultos y 550 niños. Tales inoculaciones fueron seguidas por mucho menos reacciones y menos severas que en las seguidas al uso de los toxoides ordinarios. La inmunidad por estos conferida parece adecuada y duradera a juzgar por una serie de titulaciones de antitoxina durante el curso de un año.

Lederle Laboratories Division, American Cyanamid Co.

CONGENITAL ALVEOLAR DYSPLASIA

A Developmental Anomaly Involving Pulmonary Alveoli

By H. EDWARD MACMAHON, M.D.
Boston, Mass.

THE name "congenital alveolar dysplasia" has been chosen to designate a little known congenital malformation of the lungs involving primarily the alveoli. The number of alveoli is reduced, their walls are too thick, and their spaces too small. Both lungs can be diffusely involved and this anomaly, though variable in distribution and degree, can be very marked. In respect to pathogenesis, the lesion suggests a very early defect or retardation in alveolar development. At the present time its etiology is unknown. It has been found in infants born prematurely and in children born at term. It has also been found, though in lesser degree, in full term children who have lived for weeks. This alveolar anomaly can lead to death within the first 24 or 48 hours of life; if, however, the pulmonary changes are less pronounced the child may survive, but lungs showing this anomaly appear to be predisposed to infection, since pneumonia in the first few days or weeks of life has been a common and fatal complication. Congenital alveolar dysplasia is very commonly associated with atelectasis. This may explain why this anomaly has been so generally overlooked. These two conditions have not been carefully separated and because they are so frequently confused and so often combined, it seems important that the nature and limitations of each should be clearly defined.

ATELECTASIS

The term atelectasis is used rather loosely to designate collapse or diminution in volume of pulmonary alveoli. It is also employed to denote a state of incomplete expansion of alveolar spaces that have not been previously dilated. In each case there is defective ventilation and in most cases there is a concentration of capillaries with the result that the involved area becomes deeper red and more cyanotic than the surrounding areated lung tissue. In its simplest form, atelectasis represents nothing more than an alteration in the physical state of healthy, normally developed lung tissue. It may be found alone, but is often followed by congestion, stasis, edema, bleeding or infection. On the other hand, atelectasis can be quickly superimposed on a number of pre-existing pulmonary lesions, complicating an already complex histologic picture. There is a type of atelectasis that appears and progresses concurrently with the development of a number of pulmonary conditions associated with a widening of the alveolar wall. One sees this for example in chronic interstitial pneumonia, in leukemic infiltrations into the lungs, and in tumors that extend along the walls of the alveoli. In each case the wall is widened at the expense of the alveolar space which becomes correspondingly reduced in volume. A somewhat similar picture may be seen in lungs showing congenital alveolar dysplasia for in this, as a result of defective development, the alveolar spaces remain abnormally small and their walls appear correspondingly thickened.

When the lung parenchyma of a late premature or full term child is not fully ex-

From the Department of Pathology, Tufts College Medical School, and the Boston Floating Hospital.

(Received for publication January 28, 1948.)

FIG. 1. Lung of infant. This field was selected to show atelectasis resulting from a metastatic Wilms tumor that is visible in the upper left hand corner of the field. The tumor blocked a bronchus and mechanically compressed the surrounding alveoli. Note that, although alveoli are flat and airless, their walls and spaces can still be clearly seen. (H&E, × 100.)

FIG. 2. Lung of eight-month-old stillborn premature infant showing "fetal atelectasis." Alveoli are evenly distributed and they are of an even size. Their walls are thin, delicate and wrinkled. Shape and pattern of the alveolus is well preserved. (H&E, × 100.)

FIG. 3. Lung of a premature, five-month-old stillborn fetus showing unexpanded and immature lung tissue. Alveoli are evenly distributed. Spaces are small and walls are thick. (H&E, × 100.)

FIG. 4. Lung of premature five-month fetus who lived for several hours. This field was selected to show dilatation of alveolar ducts in contrast to lack of expansion of immature alveoli. Walls of the alveoli are thick and are lined by nests of alveolar cells and capillaries. Their spaces contain little fluid. (H&E, × 100.)

panded it is commonly referred to as "congenital atelectasis," "fetal atelectasis" or "atelectasis of the new born." These three terms seem to be used interchangeably and when any one is used alone it is assumed that for the age of the child the lungs have developed normally, that they are expandable and that they are free of any other pulmonary lesion. This is often seen in cases of stillbirth and it is a common and important finding in the lungs of full term infants who may have lived for hours. The histology of this is interesting in that the alveoli tend to retain their normal pattern which is in striking contrast to the changes in shape of the alveoli that are seen in cases of severe compression (Fig. 1). The alveolar spaces are simply incompletely expanded and their thin delicate walls remain slightly wrinkled (Fig. 2). This form of atelectasis is considered to be symptomatic rather than ideopathic and paralysis or injury to the respiratory center, damage to the cord, obstruction of the trachea or bronchus or weakness of the muscles of respiration are generally accepted as the principal underlying causes. In a still earlier period of alveolar development and up until the sixth month of gestation the alveolar walls are normally so thick and coarse that the alveolar spaces are not easily expandable (Fig. 3). For example, in examining lungs of infants born during the fifth and six month of gestation who have lived for several hours, it is common to find the alveolar ducts distended with air and the alveoli unexpanded (Fig. 4). Since atelectasis is considered to be a pathologic condition it seems unreasonable to consider these very immature lungs as being atelectatic, as this unexpanded state is quite normal for this very early period in development. This picture of the early fetal lung showing dilated alveolar ducts surrounded by small unexpanded alveoli offers a reasonable explanation for the cyanosis and asphyxia that are so common at that early age. These findings are also of interest in considering the histology of congenital alveolar dysplasia, since this early immature lung has much in common with the lungs of full term infants who show this particular alveolar anomaly.

Congenital Alveolar Dysplasia

Congenital alveolar dysplasia is a congenital malformation of the lungs, or perhaps it would be better to say, it represents a group of developmental anomalies of varying degree involving pulmonary alveoli. Grossly, lungs showing this condition may appear well formed. They are as large or larger than normal and they are usually firm, rubbery and red. After the sternum is removed they seem to fill out each pleural cavity. The lungs show little crepitation and they seem almost airless. When placed in water the whole lung may float or remain suspended below the surface of the water. Small snippings may sink to the bottom at once or remain floating on the surface. Each lung weighs 10 to 15 gm. above the average. They are fleshy and like the spleen and liver, they may be cut easily when fresh into thin parallel sections. The cut surfaces are dark red, homogeneous and moist.

The lungs resemble those showing fetal atelectasis complicated by congestion and edema. They also look very much like lungs that have become distended with amniotic fluid or with an inflammatory exudate. If there is much hemorrhage, and this can be very severe in congenital alveolar dysplasia, the gross findings may resemble those of any lung showing widespread pulmonary bleeding. An accurate gross diagnosis of any of these pulmonary conditions at this early age can be very difficult. A satisfactory diagnosis of congenital alveolar dysplasia is even more hazardous since this anomaly in the gross may be completely obscured by the atelectasis with which it is so commonly associated.

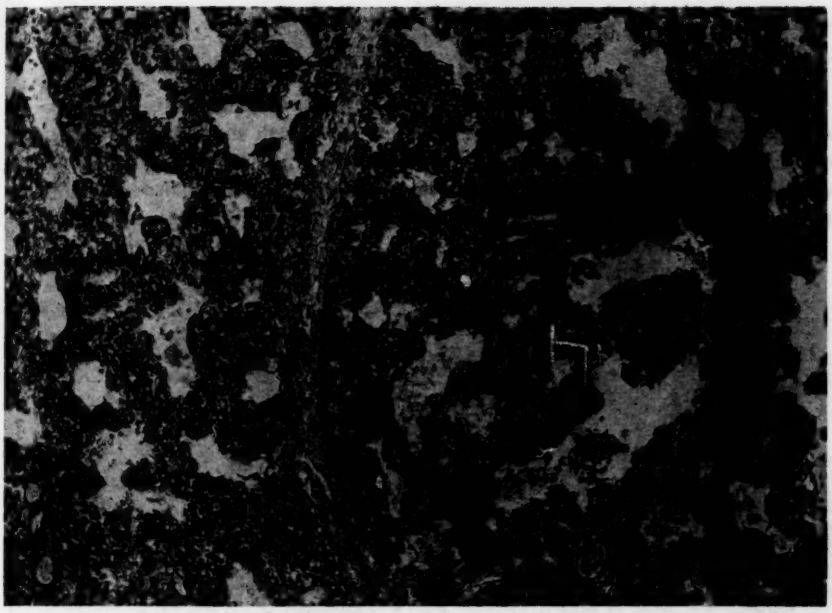


FIG. 5. Lung of full term child showing congenital alveolar dysplasia. Portions of two lobules are separated by an interlobular septum. There are few alveolar ducts and these are semi-collapsed and contain fluid. Little fibrinoid material partially coats some of these spaces. Walls bordering these spaces are thick and devoid of cuboidal cells. (EMB, × 100.)

FIG. 6. Lung of full term infant showing congenital alveolar dysplasia. There is maximal dilatation of alveolar ducts with air, with compression of surrounding lung tissue. (EMB, × 100.)

HISTOLOGIC FINDINGS

When the lungs are examined histologically the most striking changes are found to involve the alveoli and their walls. There are too few alveoli and there is too much interstitial tissue (Fig. 5). This picture may vary from field to field, particularly when it is complicated by atelectasis, congestion, edema, hemorrhage or inflammation. In its extreme form the lung seems to be composed of an excess of embryonal but highly vascularized mesenchymal tissue containing numerous well formed bronchi and bronchioles that lead into branching alveolar ducts. Most bronchioles are patent and empty, but some are collapsed and rarely one is found obstructed by disintegrating desquamated epithelial cells held in a fibrinoid exudate. Many of the ducts are coated internally by a dense, granular, eosinophilic fibrinoid exudate, and while some of these contain fluid, others are overdistended with air (Fig. 6). The total number of alveoli is greatly reduced.

FIG. 7. Lung of eighth-month premature infant showing congenital alveolar dysplasia. Histology here is comparable to that of a five- to six-month-old fetus, except that alveolar walls are not lined by cuboidal epithelial cells and that the stroma contains infinitely more capillaries than are found during that early period of development. In this field the interlobular septa and pleura are unduly conspicuous. (H&E, × 100.)

In other cases in which the changes are less severe, the histologic picture superficially resembles an immature lung of about the fourth or fifth month of gestation (Fig. 7). There are many resemblances but these two conditions are not identical. In the immature lung there are few alveoli and these are evenly distributed and their walls are thick and they are lined by cuboidal epithelial cells. In congenital alveolar dysplasia there are

also relatively few alveoli, but these are neither evenly distributed nor are they lined with cuboidal epithelial cells; instead, they are bordered by richly vascularized mesenchymal tissue interrupted here and there by small inconspicuous nests of flattened epitheilal cells (Fig. 8). Some of the alveoli are overdistended while others are completely collapsed, but common to all is an excess of interalveolar mesenchymal tissue. This connective tissue in congenital alveolar dysplasia is rich in that type of mucinous ground

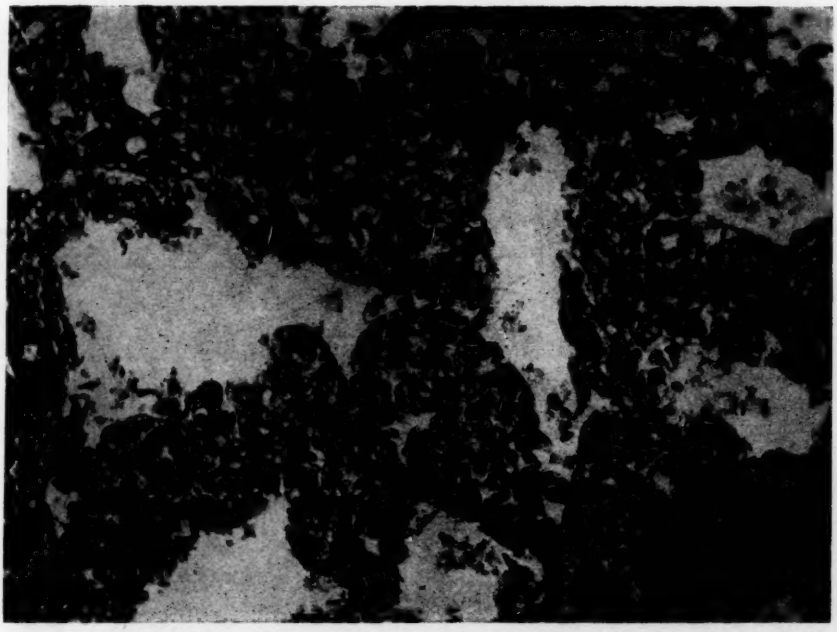


FIG. 8. Lung of full term infant showing congenital alveolar dysplasia. There are about six half distended alveolar ducts and some of these are lined with a fibrinoid exudate. They contain fluid. Adjacent tissue is composed of abnormally thick walls rich in capillaries. In this primitive connective tissue there are very few collapsed alveoli. None of these are lined with cuboidal cells. The alveolar walls are neither normally formed nor are they normally distended. (EMB, × 232.)

substance that is so conspicuous in the very primitive lung and, like the early fetal lung, it contains neither mature collagen nor elastic tissue fibrils. It is of interest, however, that this tissue possesses infinitely more capillaries than are to be found during the early period of immaturity.

In addition to these alveolar changes, there are less conspicuous and less constant changes involving the interlobular connective tissue, the pleura, and the larger blood vessels. Abnormally broad tracks of loose edematous connective tissue may separate one lobule from another and encase the periphery of the lungs, and many of the arteries are surrounded by abnormally thick adventitial columns of collagen. In two cases, the interstitial tissue throughout the lungs showed erythroblastic erythropoiesis.

This picture of a large lung composed of an excess of primitive but highly vascu-

larized interalveolar mesenchymal tissue, a diminished number of alveoli and many overdistended alveolar ducts constitutes the essential findings in congenital alveolar dysplasia.

The Complete Anatomic Pattern

In fatal cases, a number of interesting changes are found at autopsy in other organs in association with this anomaly and to visualize the regional and systemic manifestations of this deformity in their entirety, these should be briefly considered. The pulmonary artery, right ventricle, right auricle and larger systemic veins are found to be distended

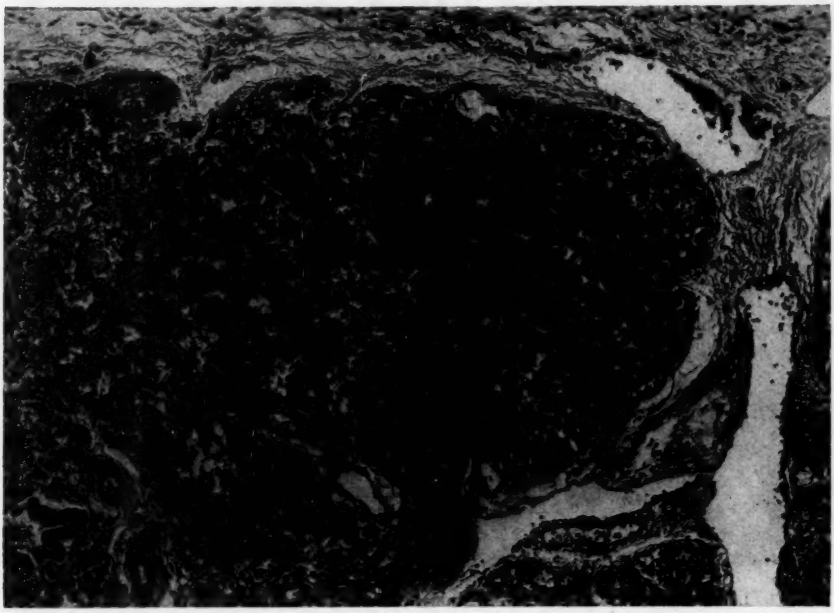


Fig. 9. Lung of full term infant showing congenital alveolar dysplasia. This field was selected to show an almost solid area of atelectasis. Stroma is abundant and abnormally rich in capillaries. Alveolar spaces are barely perceptible and these contain little fluid. Walls are abnormally thick and are completely devoid of cuboidal epithelial cells. Pleura and interlobular septa are thick and lymphatics are overdistended. (EMB, × 100.)

with blood. The left ventricle is cyanotic, somewhat dilated and flaccid and the pulmonary veins are engorged. Most of the organs are congested and edematous and the skin, lips and finger nails are blue. Capillary hemorrhages into the brain, serosal surfaces and into many other organs are common. Lastly, the intestines may be greatly distended with air which further embarrasses respiration by pushing the diaphragm upward. It will be recognized at once that all of these findings comprise the usual anatomic picture associated with almost any type of asphyxia in the newborn.

Pulmonary Complications

There are several common pulmonary complications of congenital alveolar dysplasia. These are atelectasis, congestion, edema, hemorrhage, bronchiolitis and pneumonia—

particularly aspiration pneumonia. At times one or all of these may so completely dominate the field as to obscure the essential underlying developmental anomaly (Fig. 9, 10, 11 and 12).

Functional Significance of Congenital Alveolar Dysplasia

It is difficult on morphologic grounds alone to estimate the functional capacity or incapacity of any organ. This is especially true when one is considering an organ that is the

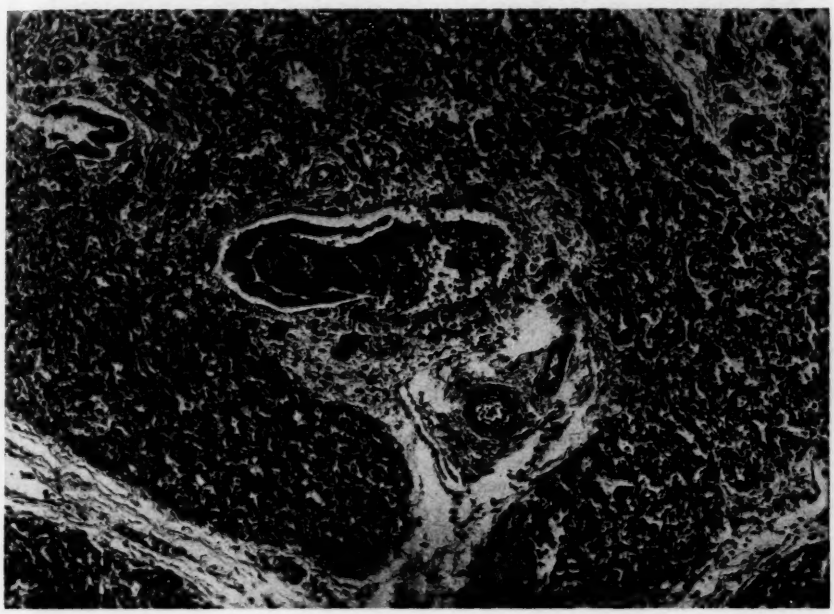


Fig. 10. Lung of full term infant showing congenital alveolar dysplasia. This field is from a larger area of atelectasis. In the center of the field there is a bronchiole filled with a cast of disintegrating epithelial cells embedded in a fibrinoid eosin-staining substance. There is no orderly arrangement to the collapsed alveoli. Lumina for the most part are empty. Walls are thick, but there is no cuboidal epithelium lining the alveolar spaces. (EMB, × 100.)

seat of a developmental anomaly. The autopsy findings in fatal cases of congenital alveolar dysplasia, however, have been of help in determining the functional significance of this entity. First, there are the changes in the lung that vary in degree from case to case; second, there is the marked dilatation of the right ventricle; and, third, there are the signs of asphyxia. These three are intimately related. Not only do the lungs show an inadequate number of thick-walled alveoli, but equally important is the fact that these lungs show little or no resilience. These structural changes alone impair respiration and lead to anoxia and they increase the load of the right ventricle. In evaluating the significance of this particular anomaly, there is another factor that should not be forgotten. The full effect of this malformation is being felt at a very critical period in the respiratory-circulatory reorganization of the infant, and at a time when the oxygen demands of the child are increasing rapidly.

FIG. 11. Lung from full term infant showing congenital alveolar dysplasia, and complicated by edema and hemorrhage. In this field the alveoli are filled with a fluid exudate rich in protein and containing scattered red blood cells. Walls of the alveoli are moderately thick and alveoli are fairly evenly distributed. This picture suggests a state of simple immaturity. (EMB, × 100.)

CLINICAL FINDINGS

A study of the clinical records of children who have died with this malformation reveals a striking similarity in all case histories. A child may cry and breathe immediately after birth, and for a variable period of minutes to hours there may be no appreciable respiratory distress. Later, breathing becomes progressively distressing and the child then shows increasing cyanosis. The chest findings are dominated by flatness to percussion and by diminished to absent breath sounds. The X-ray picture is usually interpreted as uncomplicated atelectasis. Some of the children have died of asphyxia within the first 48 hours of birth, while others have survived for weeks. In the latter case, the original malformation has been complicated by infection and pneumonia.

CLINICAL DIFFERENTIAL DIAGNOSIS

In each case in this series in which death had been early, the only clinical diagnosis was atelectasis; and in patients dying days or weeks later, the terminal clinical picture has been dominated by pneumonia. The fact that each of these groups of infants did show an underlying pulmonary anomaly in no way belittles these clinical diagnoses, since in the first group there was a variable amount of associated atelectasis and in the second group there was demonstrable pneumonia. The important point, however, is that in each case a developmental anomaly involving pulmonary alveoli had been completely obscured

by the clinical and roentgenologic findings of atelactasis and pneumonia. It must be emphasized again at this time that no attempt is being made in this paper to underestimate the importance of uncomplicated atelectasis of the newborn, but rather to point out that a developmental anomaly involving pulmonary alveoli can produce a clinical picture that is indistinguishable from it.

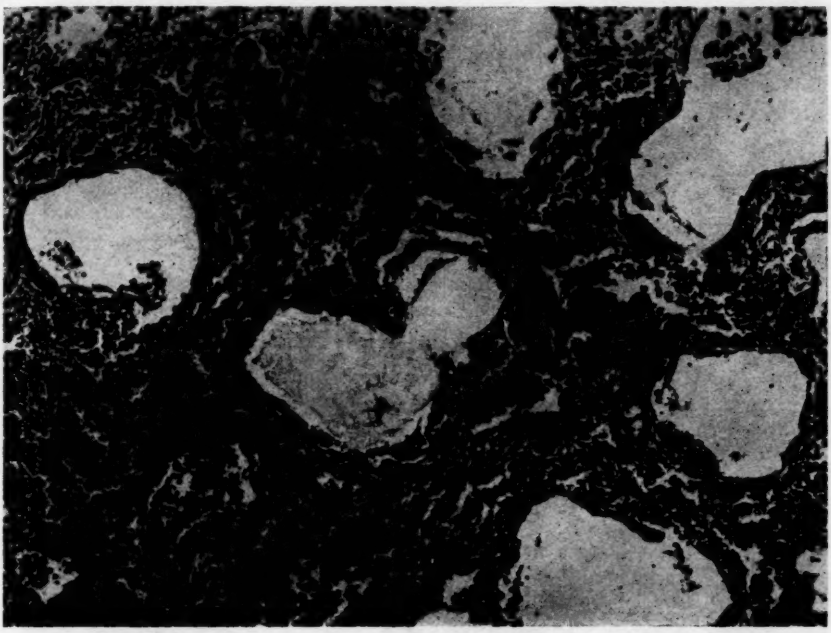


FIG. 12. Lung of full term child showing congenital alveolar dysplasia complicated by atelectasis and pneumonia. Several distended alveolar ducts containing air and fluid lie embedded in a solid sea of interstitial tissue and partially collapsed alveoli filled with polymorphonuclear leukocytes. (H&E, × 100.)

PATHOGENESIS

In its simplest form the histologic picture resembles the pulmonary pattern that one finds during the fourth and fifth month of intrauterine development. Growth of the lung is unusually well advanced, but the alveolar development is greatly retarded. At other times the problem of pathogenesis is more difficult to unravel. Epithelial development may appear to have progressed only as far as the early formation of alveolar ducts, whereas the stroma may be far in excess of normal. In the latter case, it is difficult to know whether one is dealing with a primary retardation in alveolar development or with a primary overgrowth of pulmonary mesenchyme. In comparing lungs showing congenital alveolar dysplasia with those that are normally developed, it is important to recall that in the normal process of growth and development of the alveoli their number continually increases and their walls become progressively narrow. At the seventh month of intrauterine life, the alveolus if normally developed, will have a thin and delicate wall and at this time it is indistinguishable from the alveolus of a full term infant. What-

ever the pathogenesis of congenital alveolar dysplasia may be, it appears to have its origin at a very early age in fetal development (Fig. 13, 14, 15 and 16).

Etiology

At the present time it must be admitted that the cause or causes of this condition are unknown. This anomaly has been found alone and also in combination with many other anomalies, but there has been no constant somatic linkage. It has been found in a mongolian idiot showing multiple congenital malformations. It has been seen in uniovular

Fig. 13. Lung of ten-week-old fetus. Miscarriage. At this age the mesodermal stroma far exceeds the epithelial element. Bronchi are very primitive. Stroma is rich in mucin, but almost devoid of capillaries. (EMB, × 100.)

twins. It has been found in infants showing Rh incompatability. The sexes are about evenly divided. Occasionally, there is a history of early maternal infection, malnutrition, toxemia or recurrent staining at about the third or fourth month of gestation. In one particularly striking case the mother had suffered a massive and almost fatal duodenal hemorrhage during the third month of pregnancy. In brief, nothing has been found to suggest a constant intrinsic or extrinsic etiologic factor.

Discussion

No attempt is being made in this paper to describe a new and rare condition, but one that will have been seen, though perhaps not always recognized, by anyone who has performed a number of autopsies on new born infants. Cases showing this anomaly are

FIG. 14. Lung of twelve-week-old fetus. Miscarriage. There is little difference between the character of the epithelium of the bronchi and that of the alveolar ducts. Cilia are just beginning to appear in the bronchi. There is an abundance of mucinous mesodermal tissue but very few capillaries. Lymphatics are just appearing as if by lysis of ground substance. Pattern of this very immature lung is somewhat comparable to that of the lung of a full term infant showing severe congenital alveolar dysplasia. (H&E, × 100.)

usually diagnosed as atelectasis or resorptive atelectasis, but it must be admitted that a fruitless search has usually been made in these cases in an effort to find a primary cause. In very good reviews of the problem of atelectasis of the new-born, to which the reader is referred for complete bibliography, Farber and Wilson,[1] and Potter and Adair[2] have discussed some of the difficulties in interpreting the histology and gross appearance of the lungs at this early age. In early prematurity the problem of interpretation becomes even more difficult. Farber and Wilson pointed out that not only in early prematurity but also late in intrauterine life when sufficient lung tissue may have developed to maintain life, areas of incompletely formed pulmonary tissues may still be demonstrated in proportion to the degree of immaturity of the child. They designated these areas of incompletely formed pulmonary tissue as "anectatos," "to denote the lack of capability of expansion," to distinguish them from atelectasis. Their description of these areas which they consider to be normal for the premature child has features in common with congenital alveolar dysplasia.

While the histology of this condition is of considerable academic interest as a problem in dysontogeny, and the significance of this anomaly to the infant is obvious, it is also of considerable practical importance to both physician and parents. In the past there

have been times when the clinical diagnosis of atelectasis of any type has seemed inadequate as an explanation for death, and now if one can demonstrate this primary congenital anomaly in the lung in some of the cases of asphyxia of the new-born, both physicians and parents will have a better understanding of the problems involved.

FIG. 15. Lung of 16-week-old fetus. Stillborn, miscarriage. Alveoli are small and evenly distributed. Their walls are thick and partly lined by cuboidal epithelial cells. Capillaries are already appearing along the inner and bare surface of the alveolar space. This picture is comparable to that of a lung at term showing moderate congenital alveolar dysplasia. (H&E, × 100.)

SUMMARY

A morphologic anomaly of the lungs of new-born infants has been described. It is commonly associated with atelectasis and can be responsible for atelectasis. These two conditions are often confused. It is suggested that this anomaly is an expression of retardation in normal alveolar development. It may lead to death by asphyxia, and children who survive seem unusually susceptible to pneumonia. The etiology is unknown. The term "congenital alveolar dysplasia of the lungs" has been suggested to designate this form of anomaly involving pulmonary alveoli.

REFERENCES

1. Farber, S., and Wilson, J. L., Atelectasis of the new-born, Am. J. Dis. Child. **46**:572, 1933.
2. Potter, E. L., and Adair, F. L., Fetal and Neonatal Death, The University of Chicago Press, Chicago, Ill., 1940.

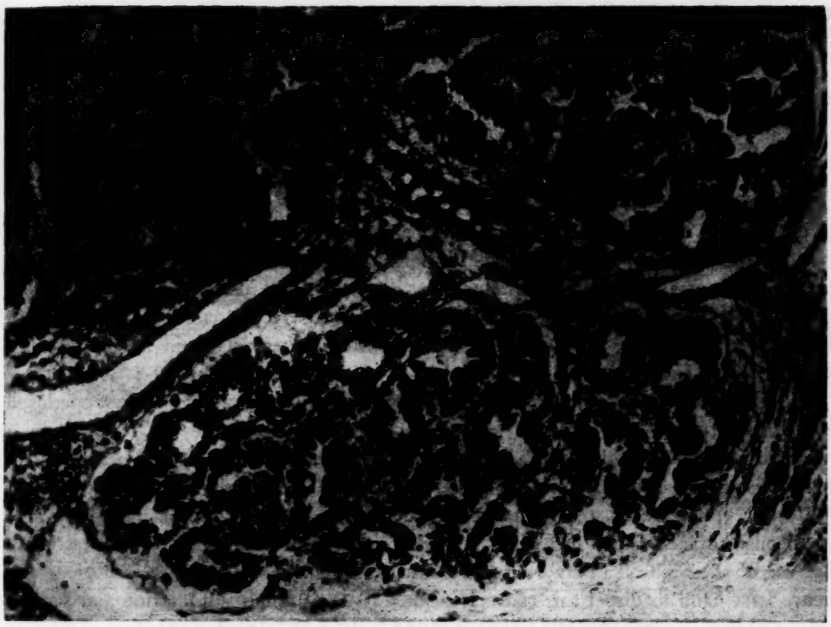


FIG. 16. Lung of a five-month-old fetus. Infant lived for several hours. This portion of lung is not dilated. Alveoli are thick-walled and lined by cuboidal epithelium. Their pattern offers a glandular appearance. There are few capillaries in the stroma and here and there solid nests of cells appear to be budding from the alveoli. The ratio here between alveolar space and wall is similar to that of congenital alveolar dysplasia, but in this lung the epithelium and capillary growth correspond to the age of the infant. (EMB, × 100.)

SPANISH ABSTRACT

Displasia Alveolar Congenita de los Pulmones

Este trabajo describe un trastorno en el crecimiento y desarrollo del alveolo pulmonar caracterizado por una desproporcion entre el tamaño de los espacios alveolares y el espesor de sus pareces. Las pareces son tambien delgadas y los espacios tambien pequeños. La resonancia esta disminuida y la circulacion pulmonar inaparente. En la opinion del autor esta anomalia que se encuentra en los prematuros y en fetos a terminos puede conducir a cianosis progresiva y muerte dentro de las 48 horas de vida. La etiologia de estas lesiones es oscura pero su patogenia parece estar ligada a trastornos del crecimiento asociados con retardos en el desarrollo alveolar.

416 Huntington Ave.

SUBCUTANEOUS ADMINISTRATION OF A SULFADIAZINE-SULFAMERAZINE COMBINATION IN CHILDREN

By LAWRENCE B. SLOBODY, M.D., DAVID LEHR, M.D., AND MILTON M. WILLNER, M.D.
New York, N.Y.

IN THE treatment of children with sulfonamides, it often becomes desirable to employ parenteral routes of administration. In infants particularly, oral administration has many decided drawbacks. The medication may be partly or completely refused. In addition, vomiting, a frequent accompaniment of acute infections, often results in the loss of some or all of the administered drug. Such loss will also be encountered in the presence of diarrhea. Hence, the uncertainty and inaccuracy attending oral dosage in infants, has led to the use of parenteral administration, especially in the acutely and severely ill patient.

In infants the intravenous route entails technical difficulties, and unless employed as a drip infusion, may result in undesirably high initial blood levels, followed by a rapid drop below the therapeutic range. Intraperitoneal injection has also been used. It establishes a more evenly sustained blood level, but is a potentially dangerous procedure (infection, puncture of the gut). Equally good results have been achieved by subcutaneous administration. For some time this route was believed to be impracticable because of the high alkalinity of the sodium salts of many sulfonamides. Sufficient evidence is at hand to dispel this conception, at least for sodium sulfadiazine and sodium sulfamerazine. Jorgenson and Greely[1] in 1942 used a 5% aqueous solution of sodium sulfadiazine without deleterious local effects. Janeway[2] and Glaser and Lawrence[3] also studied subcutaneous sulfonamide administration. Recently Clarke[4] reported on a comparative investigation of various methods of administering sulfonamides and found the subcutaneous route excellent. Yet, considering the wide application of sulfonamide therapy and the need for a variety of routes of administration, comparatively little attention has been given to the subcutaneous route.

Since it has been shown previously[5–9] that it is possible to lessen the incidence of renal complications substantially, and to achieve excellent therapeutic results by the oral administration of sulfonamide combinations instead of single compounds, it appeared of interest to investigate the practicability of giving mixtures of sulfonamides by the subcutaneous route. The present report deals with studies of the absorption and excretion, and the therapeutic application of a sulfadiazine-sulfamerazine combination administered by this route. Also included are experiments on the absorption and excretion of a sulfadiazine-sulfathiazole mixture.

THE ABSORPTION AND EXCRETION OF SULFONAMIDE COMBINATIONS

The main purpose of these studies was to ascertain the longest possible interval between two injections of a chosen dosage which would guarantee the maintenance of adequate blood levels. A single injection was given into the antero-lateral aspect of the

From the Department of Pediatrics and the Department of Pharmacology, The New York Medical College, Flower and Fifth Avenue Hospitals.

This investigation has been aided by a grant from the Schering Corporation, Bloomfield, N.J.
(Received for publication May 9, 1948.)

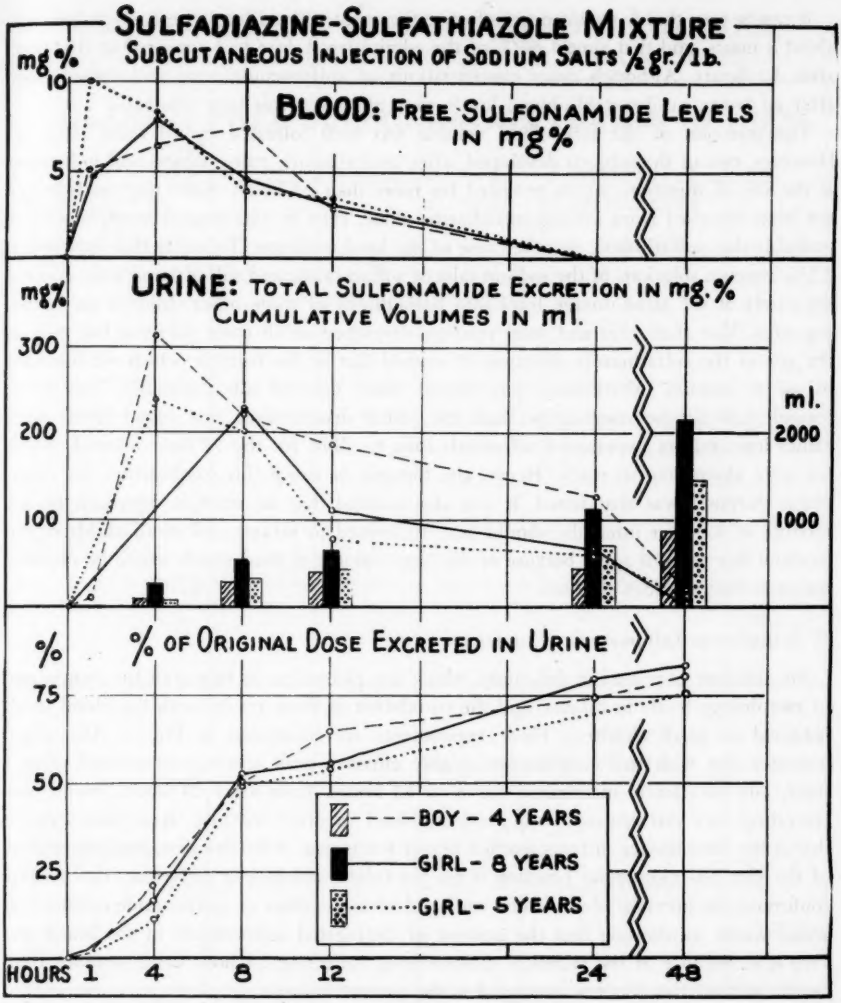


FIG. 1

thigh. Equal amounts of two sulfonamides were used. The sodium salts were dissolved separately in sterile distilled water in 5% concentration and then mixed, using equal volumes so that the final concentration of each sulfonamide was 2.5%.

A. Sulfadiazine-Sulfathiazole Combination:

Three children received the sulfadiazine-sulfathiazole combination on the basis of 0.065 gm./kg. body weight (Fig. 1). Blood levels and total cumulative urinary elimination were determined at the intervals indicated in the graph, which also demonstrates in its lower third, the urinary excretion expressed as percentage of the administered dose.

It can be seen that with this dose, effective therapeutic blood levels were maintained for about 8 hours, and that almost 60% of the administered dose had appeared in the urine after 12 hours. Although urine concentrations of sulfonamide were still considerable after 24 hours, no detectable blood levels were present at this time interval.

The injection of the large fluid volume was well tolerated by all three children. However, two of the subjects developed, after several hours, pain, redness and induration at the site of injection, which persisted for more than 24 hours. Since this reaction had not been observed from sodium sulfadiazine alone, even in 5% concentration, it seemed probable that sulfathiazole was the cause of the local irritation. To verify this contention, 2.5% aqueous solutions of the sodium salts of sulfathiazole and sulfadiazine were injected separately at the same dosage level into both thighs of three other children on opposing sites. This time pain and local reaction developed in all three subjects, but only at the site of the sulfathiazole injection. It seemed that in the form in which we intended to use it, sodium sulfathiazole was irritant when injected subcutaneously. The sulfathiazole-sulfadiazine combination had the added disadvantage that blood levels were rather low and not maintained sufficiently long to allow for the 12 hour interval, which we were attempting to reach. Hence, the thought of using this combination for therapeutic purposes was abandoned. It was also realized that intermittent injections of any mixture at 12 hour intervals, should best be limited to infants and small children (up to about five years of age), because of the large volume of fluid which would be required for each dose in older children.

B. Sulfadiazine-Sulfamerazine Combination:

Six children were used in this study, which was planned so as to permit the comparison of two dosage levels in infants, and the correlation of these results with the blood levels obtained in small children. These experiments are illustrated in Fig. 2. The graph indicates that with this combination, highly effective peak levels were reached after 1 hour, and excellently maintained for 8 to 12 hours. Even after 24 hours, blood concentration was still around 4 mg./100 cc. blood in every instance. It is also apparent that at the same dosage, infants reached higher levels than older children, possibly because of the fact that glomerular function is not yet fully developed in early life. This finding confirmed our previous observations with oral administration of sulfonamide mixtures. It seems worth mentioning that the amount of conjugated sulfonamide in the blood was very low. Because of the technical difficulties of collecting 24 hour urine samples from small children, this was not attempted in the present instance.

THE THERAPEUTIC USE OF A SULFADIAZINE-SULFAMERAZINE COMBINATION

Treatment with a mixture containing equal parts of sulfadiazine and sulfamerazine was carried out in 60 unselected childen (age: newborn to five years), with acute bacterial infections including meningococcal and influenzal meningitis. bronchopneumonia, lobar pneumonia, otitis media, follicular tonsillitis, enteritis, and sepsis of the newborn. In this work we were not primarily attempting to prove the therapeutic efficiency of sulfonamide combinations, since this had been done adequately.[6,7,8] Rather it was desired to demonstrate the feasibility and practicability of intermittent subcutaneous administration of sulfonamide combinations and to establish definite rules for dosage and intervals of administration.

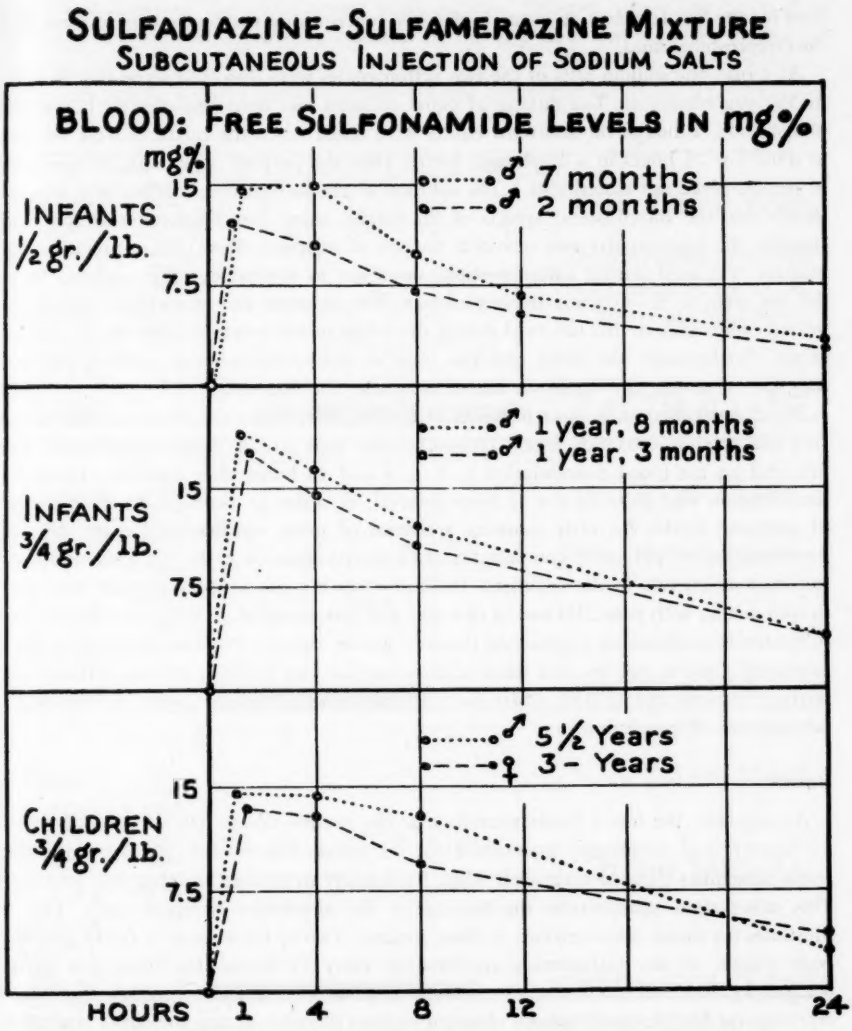


FIG. 2

Procedure:

With regard to routine clinical procedures and hydration, the same general plan was followed as described in detail in a previous publication.[7] Concerning dosage, we decided on the following schedule, based on the experience of the absorption-excretion study. The sulfadiazine-sulfamerazine combination, consisting of equal amounts of both drugs, was injected subcutaneously in the total dosage of 0.065 gm./kg. body weight every 12 hours throughout the course of therapy. Only in severe infections, particularly in meningitis, was it felt that a higher does, 0.1 gm./kg. should be given at each interval, at

least for the first few days, to insure high tissue concentrations and adequate diffusion into the cerebrospinal fluid.

As a rule, the sodium salts of the two sulfonamides were dissolved separately in water in 5% concentrations. The mixing of equal volumes was done immediately before administration, although no untoward effects were noted when the mixtures were allowed to stand for 24 hours in a diaphragm bottle. (For the purpose of storage, refrigeration of the dissolved salt is desirable.) The solution of the sulfonamide mixture was injected slowly into the antero-lateral aspects of the thighs, using each thigh alternately. Occasionally, the interscapular area served as the site of injection. Slow, steady pressure with massage was used during administration, so as not to distend the skin unduly. There did not seem to be any great amount of pain. The duration and character of crying appeared comparable to that observed during the subcutaneous administration of physiologic saline. Furthermore, the older children used in absorption-excretion studies, did not complain of severe pain during or immediately after the injection.

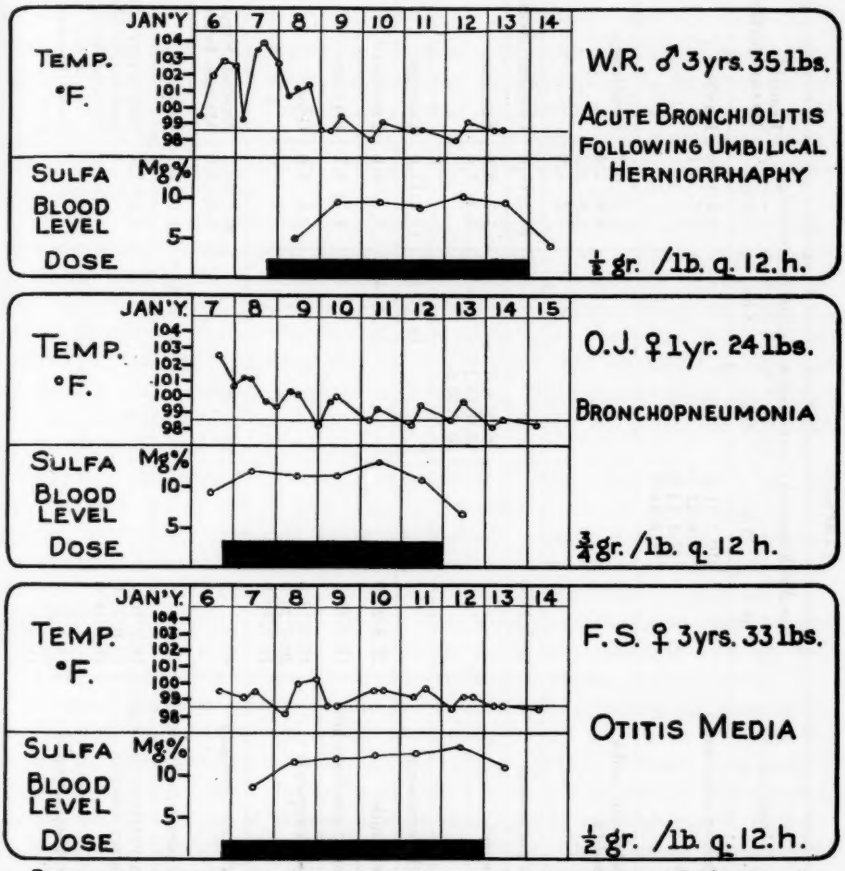
Blood was collected in most instances at least once daily for the determination of the free and total sulfonamide level. The collections were so timed that information was procured on the blood concentration 2, 4, 6, 8 and 12 hours after injection. Particular consideration was given to the 12 hour interval, in order to ascertain the maintenance of adequate levels. An early morning specimen of urine was obtained every day for determination of pH, drug concentration and the presence of casts, red blood cells, or sulfonamide crystals in the sediment. In some cases the sulfonamide mixture was used in conjunction with penicillin and in one case with streptomycin. In the great majority the sulfonamide combination represented the only specific therapy. No alkalizing agents were employed. Only in one instance when acidosis became very marked, was the sulfonamide mixture incorporated in 1/6 molar sodium-r-lactate solution and given by continuous subcutaneous drip infusion.

Results:

As expected, the blood levels were high at the routine dosage (0.065 gm./kg. every 12 hours), and excellently maintained for 12 hours. On the 0.1 gm./kg. dose, the levels sometimes climbed excessively high, particularly in infants less than one year old. This observation substantiates the finding of the absorption-excretion study. Fig. 3 illustrates the blood concentrations in three patients. Two of these received 0.065 gm./kg. body weight of the sulfonamide combination every 12 hours, the third was given 0.1 gm./kg. Since all blood levels were taken 12 hours after the last injection, the values represent the lowest concentrations obtained in these children during the entire treatment period. Conjugation figures were low, varying between 10 and 20% of the blood level. Possibly in early life the ability of the liver to acetylate sulfonamides is not yet fully developed. The therapeutic response was excellent in all three instances. No urinary crystals or any signs of renal irritation were observed, despite the fact that sulfonamide concentrations in the urine were excessively high.

Table I summarizes blood level studies and therapeutic results in 12 additional children. Again special attention was given to the sulfonamide concentration 12 hours after subcutaneous injection, but frequent determinations were made also at various intermediate intervals, in order to gain information on peak levels obtainable with the proposed dosage scheme. These data suggest that the highest blood levels are reached

within two hours of the subcutaneous administration, followed thereafter by a slow decline, which approaches roughly one-half of the two hour concentration at the 12 hour interval. As expected, pronounced forcing of fluids lowered the blood levels; whereas, poorly functioning kidneys induced excessive blood concentrations (Case 9). The urine



DETERMINATIONS OF ALL BLOOD LEVELS WERE DONE 12 HOURS AFTER THE SUBCUTANEOUS INJECTION OF THE SULFADIAZINE–SULFAMERAZINE COMBINATION.

FIG. 3

concentrations ranged between 300 and 600 mg. of total sulfonamide per 100 cc. reaching at times levels of 900 mg./100 cc. Despite these high urine concentrations, only five cases developed a transient and light crystalluria. Two of these showed a concomitant microscopic hematuria, which cleared completely on cessation of therapy. As a consequence of therapy, "mild" neutropenia developed in several instances, particularly

TABLE I

Case No.	Age	Sex	gm/kg q. 12 hr.	Diagnosis	Blood Sulfonamide Concentration mg/100 cc. free/total					Remarks: Therapeutic Response:
					2 hr.	4 hr.	6 hr.	8 hr.	12 hr.	
1	10 mo.	M	0.065	Suppurative otitis media		10.7/11.8 10.0/12.5 12.7/13.8 14.8/16.2			9.6/10.6 7/5. 9.1	Excellent
2	4½ mo.	M	0.065	Purulent otitis media, Mastoiditis					6.2/ 6.2 6.4/ 7.4 6.9/ 8.2 7.2/ 7.6	Satisfactory
3	16 mo.	F	0.065	Lobar pneumonia	18.5/18.5				10.5/11.6	Excellent; Neutropenia
4	2½ yr.	F	0.065	Pneumonia			6.0/ 6.2 13.0/13.2 10.0/10.6		5.7/ 6.6 7.2/ 7.9	Excellent
5	18 mo.	M	0.065	Bronchopneumonia				14.4/15.3	11.4/12.0	Excellent
6	6 mo.	F	0.065	Acute rhinitis	21.8/22.0			13.3/14.2	7.1/ 9.6	Excellent
7	13 mo.	M	0.065	Laryngotracheobronchitis	15.3/18.5				8.7/ 8.7	Excellent
8	17 mo.	F	0.065	Bronchopneumonia	13.4/13.6 20.0/20.0 16.0/16.0				7.0/ 8.6	Good
9	10 mo.	M	0.1	H. influenza meningitis	40.0		27.2/29.7		20.1/20.7 9.0/ 9.0	Expired. Streptomycin, Penicillin, Multiple Brain Abscesses
10	4½ mo.	M	0.1	Acute purulent otitis media	27.2			19.1/20.8	12.0/14.7	Excellent
11	2 yr.	F	0.1	Primary atypical pneumonia, Secondary infection	16.2/16.2 25.0/25.0 16.0/16.0				7.5/ 7.7	Satisfactory: Sulfonamides retarded after 12 days. No sensitization noted.
12	3½ yr.	F	0.1	Acute nasopharyngitis	12.1/12.1 19.2/19.2 15.2/15.4 17.5/17.5					Good: Transient Crystalluria, Poor fluid intake.

in patients treated with the larger dosage, and consequently showing excessive blood concentrations. There were no untoward local reactions in somewhat more than 500 separate subcutaneous injections. There was one instance of drug rash and fever, in a four-year-old girl treated for meningococcic meningitis, on the seventh day of therapy.

Comments

The present study demonstrates that the use of a sulfadiazine-sulfamerazine combination by intermittent subcutaneous injection has a definite place in the treatment of infants. The procedure itself is extremely simple and harmless. It requires no intricate apparatus nor any special skill. It assures the rapid attainment and maintenance of excellent blood levels. Consequently, therapeutic results in sulfonamide sensitive infections leave nothing to be desired.

Compared to single sulfonamides employed by this procedure,[3] or by continuous hypodermoclysis,[10,11] the sulfadiazine-sulfamerazine combination appeared safer because of the low incidence of crystalluria and renal complications, despite the presence of high sulfonamide levels. In fact, as pointed out previously, on the larger dosage (0.2 gm./kg. body weight in 24 hours), the concentrations often climbed to peaks of 30 and 40 mg./100 cc. blood and more than 600 mg./100 cc. urine. And yet there were only two instances of mild hematuria in our series of 60 cases. This incidence seems not higher than would be expected if either sulfadiazine or sulfamerazine had been given separately in one-half dosage present in the combination.

Jorgenson and Greely,[1] determining blood levels in infants and children after subcutaneous injection of sodium sulfadiazine as 5% aqueous solution on the basis of 0.1 gm./kg. body weight, arrived at figures which closely resemble those that we obtained with the same dosage of the combination. Later, Glaser and Lawrence,[3] treating children with 5% sodium sulfadiazine, injected intermittently by the subcutaneous route at 12 hour intervals on the basis of 0.13 gm./kg. body weight, again obtained blood concentrations very similar to those that we found for the mixture. However, they reported "frequent crystalluria" and "some hematuria," without giving any definite figures.

Forbes and Herweg,[11] using 0.5% solutions of sulfadiazine could maintain blood levels in the neighborhood of 10 mg./100cc. when using 0.2-0.3 gm./kg. in 24 hours. In patients for whom blood levels of 20 to 30 mg./100 cc. appeared desirable, these authors suggest the use of 0.4 to 0.5 gm./kg. in the first 24 hours. Similar findings were reported for the subcutaneous use of sulfamerazine by Forbes, Perley and Dehlinger.[10] In order to obtain blood concentrations of 25 to 30 mg./100 cc. while treating patients with meningococcic meningitis, the authors administered 0.5 gm./kg. of sodium sulfamerazine as a 0.5% solution on the first day and continued with a daily dosage of 0.3 gm./kg.

They found mild, but relatively frequent toxic reactions in 135 children treated with sulfamerazine alone by various routes although average blood levels were not higher than 10-15 mg./100 cc. Aside from drug fever, rash, "mild" leukopenia, anemia, anorexia, and vomiting, microscopic hematuria occurred rather frequently (12.6%) in spite of adequate alkalization of the urine. Gross hematuria was observed twice and albuminuria and oliguria once. In general, the authors conclude, the frequency of reactions was about equal to that observed previously with sulfadiazine.

Obviously the method of Forbes and associates is not directly comparable with our procedure. Using sulfonamide solutions only one-tenth the concentration of ours by the

drip infusion technic, they could avoid the spiking of blood levels caused by intermittent injection and insure adequate hydration at all times, which constitutes a decided advantage. The procedure used by us, on the other hand, seems just as effective from a therapeutic standpoint, and is conspicuous because of its simplicity. If necessary it can be carried out in the patient's home, since no particular attention is required throughout the 12 hours following each pressure clysis. In comparing renal complications, our procedure must be considered at a disadvantage because of the high blood level peaks within the first few hours after each injection and because of the omission of adjuvant alkali therapy. In the light of these considerations, the low incidence of hematuria observed in our admittedly small series, assumes added significance. It can be explained only on the basis of the protection afforded to the kidney by sulfonamide combinations.[5]

With regard to allergic reactions, our observation of one instance among 60 patients, is in decided contrast to the incidence of 15.6% of "drug rash, drug fever, and/or conjunctivitis," reported by Zeller and associates[12] in 75 cases of meningococcic meningitis treated with a sulfadiazine-sulfamerazine combination. The fact that these authors used dosages "25-30 per cent" above the routine dosages for comparatively long treatment periods, would seem insufficient to account for their high figure of sensitization reactions. Their finding may be due to the inclusion of non-allergic conjunctivitis which frequently accompanies meningitis. It should be pointed out that conjunctivitis alone, as an allergic reaction, is known to occur occasionally from sulfathiazole, but has not been reported for sulfadiazine or sulfamerazine by other workers in this field, nor did we observe it in our years of experience with these drugs. Our point of view may help to explain the figure of 10% sensitization reactions given for sulfadiazine alone by Zeller and co-workers, which is the highest incidence for this drug that we could find in the literature. The conclusions of these authors from their series that the advantages of the sulfadiazine-sulfamerazine combination are outweighed by the disadvantage of a possible increase in allergic reactions are not borne out by our findings in this and previous studies with sulfonamide combinations,[7,8] since we did not observe any increase in the incidence of sensitization reactions.

The fact that excessive blood and urine levels of sulfonamide may be encountered on this relatively moderate dosage schedule, suggests the advisability of frequent blood level studies and urine examinations. A high fluid intake is essential and alkalization may be employed as an added safety measure, particularly with the larger dose.

Summary

The feasibility of intermittent subcutaneous administration of a sulfadiazine-sulfamerazine combination (2.5% aqueous solutions of the sodium salts in equal amounts) in infants and children was evaluated by means of absorption-excretion and therapeutic studies.

In 60 children with acute infections, intermittent injections of this combination at 12 hour intervals on the basis of 0.13 gm./kg. to 0.2 gm./kg. in 24 hours, gave excellent and well sustained blood and urine levels of sulfonamide and resulted in a highly satisfactory therapeutic response. No local reactions were encountered in more than 500 individual injections.

The incidence of systemic toxicity from the sulfadiazine-sulfamerazine combination was lower than that reported in similar treatment with either compound employed sepa-

rately. Renal complications, in particular, appear substantially decreased despite the omission of adjuvant alkali therapy. Only one sensitization reaction was observed in this series.

Because of its local irritant effect, the subcutaneous administration of sodium sulfathiazole is not recommended.

Subcutaneous therapy with a combination of sodium sulfadiazine and sodium sulfamerazine has a definite place in the treatment of the infant and small child. The combination seems preferable to single sulfonamides because of a distinctly lower toxicity. These findings confirm our previous studies with oral administration of sulfonamide mixtures.

Acknowledgements

The technical assistance of Helen and Ruth Salzberg is gratefully acknowledged. We also wish to thank Dr. Louis A. Perillo and Dr. Robert Fielding for their cooperation in this study.

References

1. Jorgenson, G. M., and Greely, D. M., Subcutaneous administration of sodium sulfadiazine, J. Pediat. **21**:325, 1942.
2. Janeway, C. C., Use of sulfonamides in treatment of respiratory infections in children, New England J. Med. **229**:201, 1943.
3. Glaser, K., and Lawrence, G., Subcutaneous administration of sodium sulfadiazine, J. Pediat. **27**:492, 1945.
4. Clarke, G. H., Sulfonamide drugs, comparison of blood levels obtained with their administration by different routes in children, Am. J. Dis. Child. **73**:565, 1947.
5. Lehr, D., Inhibition of drug precipitation in the urinary tract by use of sulfonamide mixtures; sulfathiazole-sulfadiazine mixture, Proc. Soc. Exper. Biol. & Med. **58**:11, 1945.
6. Lehr, D., Prevention of renal complications by therapeutic employment of sulfonamide mixtures; sulfathiazole-sulfadiazine combination, J. Urol. **55**:548, 1946.
7. Lehr, L., Slobody, L. B., and Greenberg, W. S., Use of sulfadiazine-sulfathiazole mixture in treatment of children, J. Pediat. **29**:275, 1946.
8. Lehr, D., Prevention of renal damage by use of mixtures of sulfonamides; Animal-experimental and clinical studies, Brit. Med. J. **2**:943, 1947.
9. Frisk, A. R., Hagerman, G., Helander, S., and Sjogren, B., Nordisk Med. **29**:639, 1946.
10. Forbes, G. B., Perley, A., and Dehlinger, J., Use of sulfamerazine in infants and children, J. Pediat. **28**:24, 1946.
11. Forbes, G. B., Donnell, G., and Herweg, J. C., Subcutaneous administration of sodium sulfadiazine, J. Pediat. **31**:375, 1947.
12. Zeller, W. W., Hirsch, H. L., Sweet, L. K., and Dowling, H. F., Treatment of meningitis with sulfadiazine and sulfamerazine, J.A.M.A., **136**:8, 1948.

Spanish Abstract

Administrations Subcutanea de una Sulfadiazine-Sulfamerazine Combinada en el Niño

La administracion subcutanea intermitente de una combinacion sulfadiazine sulfamerazine (2.5% de solucion acuosa de la sal sodica a partes iguales) en niños pequeños y mayores es considerada en este trabajo realizandose un estudio terapeutico de la absorcion y excresion.

En 60 niños con infecciones agudas, inyecciones intermitentes de estas combinaciones con 12 horas de intervalo a base de 0.13 gm. por cada g. a 0.2 gm. por cada g. en 24 horas dio excelentes concentraciones sanguineas de sulfonamida con un resultado terapeutico altamente satisfactorio. Las dosis mas pequeñas son recomendadas para los niños lactantes y las mayores para los niños de mayor edad, de mas de 2 años. Ninguna reaccion local fue observadas en mas de 500 inyecciones individuales.

Las soluciones son hechas con agua destilada mezclandola en la jeringa inmediatamente antes de la inyeccion. Se recomienda como sitio de la inyeccion la superficie anterolateral del muslo o la region interescapular. Inyecctar lentamente y practicar despues un ligero masaje. No se reporta generalmente dolo.

La incidencia de toxicidad de la sulfadiazine-sulfamerazine combinada es mas baja que la reportada en tratamientos similares empleando estos compuestos separadamente. Complicaciones renales en particular parecen sustancialmente disminuidas. Solamente una reaccion de sensibilizacion fue observada en esta serie.

La administracion del sufatizol sodico no es recomendada por su efecto local irritante. La terapeutica subcutanea con una combinacion de sulfadiazine y sulfamerazine sodicas tiene un lugar definido en el tratamiento de los niños sobre todo en los niños pequeños. La combinacion parece preferirse al uso aislado o simple de la sulfonaminas porque la combinacion disminuye la toxicidad. Estos hallazgos confirman nuestros estudios previos de la administracion oral de mezclas de sulfas.

Fifth Ave. at 105th St.

OUTLINES FOR WELL BABY CLINICS

II. Recording Development of the Second Twelve Months

By EDITH S. HEWITT, M.D., AND C. ANDERSON ALDRICH, *M.D.*
Rochester, Minn.

IN 1946 we presented a description[1] and explanation of a set of cards used by the Rochester Child Health Project in its well baby clinics. These cards, it was hoped, would help the attending physicians to learn about and to record the evidences of growth and development of babies as they appear in the first twelve months of life. In this article we shall describe and explain a similar set of cards devised for use in the second year.

After the first year, growth and development are not so rapid as they are earlier; the changes from month to month are not so evident and methods of managing a child need not be altered so frequently. Therefore the mothers are asked to bring children in for conferences at fourteen, sixteen, eighteen, twenty-one and twenty-four months of age only. Thus, only five cards are needed in the second year.

The following material appears on the respective cards. Information given under the numbered headings appears on the faces of the cards; the explanatory notes are printed on the reverse.

CARD 1. SUBJECTS TO BE CONSIDERED AT THE AGE OF FOURTEEN MONTHS

1. *Development:* Baby walks; may even be able to run and climb. Pushes, pulls and piles large objects. May turn pages of a book one at a time.

2. *Habits:* Eating—Baby may have full adult diet, except for nuts, berries, fat meats and highly seasoned foods. May continue to have bedtime bottle if he desires it. Self-feeding with fingers, spoon, cup or glass should be encouraged even if result is messy.

Sleeping—Baby's night sleep may be disturbed. May take one or two naps, tending toward one.

Elimination—Bowel: Baby may indicate time for bowel movement.

Bladder: Mother may "catch" urine in toilet; if not successful, she should stop trying for two or three weeks; progress should not be forced. Mother understands meaning of "catching" from explanation given her concerning bowel control when child was in sixth month of life.[1]

3. *Social adjustment:* Baby is becoming increasingly independent; wants to help undress and feed himself; objects to play pen. Enjoys the rhythm of singing, of the radio and of being read to.

Speech—Baby can say a word or two, especially if composed of repeated syllables (mama, byebye).

4. *Physical examination:* Examiner records anything noteworthy.

Explanatory notes relative to Card 1. Development—In the second year the steps of development, although regularly progressive, are not so clearly defined as in the first year. The baby may learn to do many new tricks in a short time or he may not acquire any new

---

From Rochester Child Health Institute, and from the Section on Pediatrics, Mayo Clinic, Rochester, Minn.

(Received for publication April 23, 1948.)

skills for several weeks. The mother can be assured that, if she is patient, she will see the baby perfect many abilities that were latent or just emerging in the first year. At first, the baby becomes skillful in use of the large muscle groups, thus learning gross control over his extremities and body. Later he will show skill in the use of small muscle groups, in the intricate movements necessary to manipulate small objects. The examiner explains to the mother that through the second year the baby probably will gain less than 0.2 kg. a month and that this gain may be irregular, depending on activity, season and body build.

Eating—After the baby has grown enough teeth to enable him to chew well, and after he has learned to chew, it is not necessary to prepare food especially for him. Of course, some foods, such as meat, must be cut for him.

Elimination—Bowel: Control of defecation usually precedes control of micturition. If "catching the stool," as described in the first year,[1] is successful, the practice should be continued. If the baby indicates the time for bowel movement, his rhythm is accepted rather than an arbitrary time being imposed on him.

Bladder: About the fourteenth month, or as soon as the mother notices that the baby urinates at intervals of one and a half to two hours, she may try "catching" his urine. For this process, diapers are discarded in favor of training pants and the baby is seated on the toilet at the intervals which he has shown to be appropriate for him. However, if the baby resists sitting on the toilet, or if he does not learn to urinate as soon as he is placed there, diapers should be resumed for two or three weeks before a new attempt at "catching" is made. This may be called the "stop and go" method.

Both bowel and bladder: About this time, also, the baby's imitative ability is utilized to help control both defecation and urination. If the mother says the same word each time just before she takes the baby to the toilet, he will begin to say the word himself when he feels the need to eliminate. Several months may be required for the baby to become perfect in this adjustment, however.

Social adjustment—The baby should be encouraged to do as much for himself as he can, even though this requires much time and patience on the part of the mother. He learns by doing.

Speech: It is best that the mother not be told any particular number of words which her baby may be able to say initially. At this time she is likely to attach too much importance to the number. Later, she learns flexibility and does not worry about it.

Card 2. Subjects to Be Considered at the Age of Sixteen Months

1. *Development:* Baby climbs and jumps. Can walk backward as well as forward. Can release objects. Puts pegs in a hole in a board; builds a tower of three or four blocks.

2. *Habits:* Eating—Appetite is definitely reduced. A wide variety of simple foods should be offered him, in small quantities. The foods served most frequently are those the baby prefers. He has gained some skill with cup and spoon; may use fork.

Sleeping—Night sleep still is likely to be disturbed. Baby usually takes one long afternoon nap.

Elimination—Bowel: Baby may take responsibility for bowel control but needs assistance with clothes and seating.

Bladder: Baby may stay dry through nap.

3. *Social adjustment:* Independence increasingly noticeable. Child is angry if can't have own way; resents being handled by strangers; wishes to be center of attention.

Speech—Child may use six or eight words.

4. *Physical examination:* Examiner records anything noteworthy.

Explanatory notes relative to Card 2. Development—The baby becomes increasingly skillful in co-ordinating the relaxation of certain muscle groups and the contraction of others; this enables him to throw a ball in the desired direction. He is also increasing his skill in using the smaller muscles of the hands.

Eating—The mother should be warned again that appetite is definitely less in the second year than in the first and that she should attend to the other matters noted on this card under habits of eating so that the baby's eagerness for food will be encouraged.

Social adjustment—The baby's inability to accomplish things he tries may exasperate him; temper flare-ups are frequent. Again, patience and understanding in handling these outbursts are of utmost importance.

Card 3. Subjects to Be Considered at the Age of Eighteen Months

1. *Development:* Large movements still predominate, although increasing in variety. Improvement evident in fine movements, such as using the spoon, undressing, turning pages and so on.

2. *Habits:* Eating—Mother should not fuss; she should keep mealtime pleasant and enjoyable. Occasionally "treats" should be included.

Sleeping—Child should sleep better than before; is in a more settled period of life. Will stay under covers. Afternoon nap may be shorter than before.

Elimination—Bowel: Time for movement may be irregular.

Bladder: Mother should try to "catch" after child's nap. Child possibly remains dry through the night.

3. *Social adjustment:* Child still is interested mainly in self. Investigates others by poking, pulling, pushing. Needs mother or rest of family about; uneasy if alone.

Speech—Uses about twelve words; may put two words together.

4. *Physical examination:* Examiner records anything noteworthy.

Explanatory notes relative to Card 3. Social adjustment—As yet, the child is scarcely aware of other people as beings separate from himself. His poking, pulling and pushing at them corresponds to his method of examining inanimate objects to see how they feel, move and respond. His need for familiar company is attributable to his having as yet developed no sense of security within himself. If mother is standing by, he will attempt many new things with confidence, which he would not do if she were not there.

Card 4. Subjects to Be Considered at the Age of Twenty-One Months

1. *Development:* Child is very active; seems that he is impelled to climb and push. Perhaps he can walk up stairs, one at a time.

2. *Habits:* Eating—Usually child has given up bedtime bottle but may have it if he wants it. Likes and dislikes are shown by whims and "food jags." Usually feeds himself well.

Sleeping—Beginning of period of sleeping difficulties. Also may be fussy about going to sleep at nap time.

Elimination—Bowel and bladder: Poor control may recur; lapses are common. Boys may start to stand upright to urinate.

3. *Social adjustment:* Child prefers outdoors. Plays with increased variety of objects: sand box, wagon, climbing apparatus, and so on. Resents restraint. Ignores pointless or long admonitions. Responds best if treated with humor; not with exasperation.

Speech—Makes phrases.

4. *Physical examination:* Examiner records anything noteworthy.

Explanatory notes relative to Card 4. Eating—Preference for various foods may vary from day to day or the child may prefer one food only for several successive days ("food jags"). If the child's whims lead him to demand nutritious foods not usually provided and the mother accedes to his desires, she will aid him to develop a selective taste for a variety of foods. The aim is to develop happy eaters, not fussy ones.

Elimination—Skills are being acquired but the child is far from perfect in them. This applies to control of bowel and bladder as well as to other activities. The child is not to blame for relapses in what has seemed to be nearly perfect control. If use of diapers has to be resumed, the attitude of mother should be casual and only when the child again shows interest in training, should training again be attempted. The child is a great imitator in these matters as in all others. Observing the bathroom habits of the other members of the family may stimulate him to adopt their methods. The wish of boys to stand up to urinate may be initiated by their seeing their older brothers and father urinate thus.

Social adjustment—The child should be allowed reasonable freedom. His attention span is short and his understanding of words imperfect. This is why too much talk becomes meaningless and why orders and directions should be brief, definite, infrequent and consistent. The admonition given in the first year should be recalled; namely, to teach only one thing at a time.

Card 5. Subjects to Be Considered at the Age of Twenty-Four Months

1. *Development:* "Do it myself" is an outstanding characteristic as skill increases in manipulating objects such as shoes, buttons, spoon, fork and toys or negotiating stairs or doors, and so on.

2. *Habits:* Eating—Child likes increasing variety of foods. For most part feeds himself but may need help to finish. Stops throwing spoon. Eating alone may still work best.

Sleeping—Bedtime rituals to be expected; child is not stalling. He should be encouraged to expect bedtime no later than 8 P.M.; it should be a happy, peaceful time. Usually he takes a long nap in early afternoon.

Elimination—Bowel and bladder: Child usually can manage clothes and can go to toilet alone in daytime. Does well but may not be perfect.

3. *Social adjustment:* Child is not cooperative. Not ready to share as yet. Parallels others at play. Is a dawdler; attention transitory but more organized than before. Mother still most important person. Has learned much about conformity.

Speech: Makes short sentences.

4. *Physical examination:* Examiner records anything noteworthy.

Explanatory notes relative to Card 5. Development—Independence should be encouraged. The child should be allowed to do as much as he can safely do alone. When he becomes exasperated, he should be helped along a little until he wishes to take over the

task himself. This takes patience, as it would be much easier and quicker for the mother to do the thing herself.

Eating—This should be increasingly orderly as the child gains in expertness in feeding himself.

Sleeping—The bedtime rituals may seem endless: toilet, drink of water, the special doll, the goodnight kiss, and so on. The parent may be able to limit this somewhat but it is best to accede to most of it. As the child grows older the ritual will lessen.

Social adjustment—Before a child can be willing to share his toys, he must learn what possession means. At this age, then, he should be allowed to have his own things and not be obliged to lend them to others. He likes to play along with others but usually at his own independent occupation (parallelism). Later, he will wish to work with another child on the same project.

Purpose of the Advice Given on the Cards and Flexibility in Their Use

The advice constantly given on the cards is to synchronize care with infant growth. If followed, this advice will help children to conform. They can conform more easily if adults adjust their demands to the capabilities of the children.

As was written at the conclusion of the preceding article,[1] the cards for the second year are not offered as a rigid guide. Normal growth is variable and application of the foregoing outlines also must be flexible.

References

1. Aldrich, C. A., and Hewitt, Edith S., Outlines for well baby clinics; recording development of the first twelve months, Am. J. Dis. Child. 71:131, 1946.

Spanish Abstract

Instrucciones para Clinicas de Niños Sanos. II. Record del Desarrollo en el Segunda Año

En las edades de 14, 16, 18, 21 y 24 meses los pasos que marcan el desarrollo pueden ser notados principalmente en la habilidad motora, en la comida, en el sueño, en las eliminaciones y en los ajustes sociales del niño. Este trabajo sienta los pasos dicernibles en los varios meses y la manera como el examen fisico puede ofrecernos detalles recogidos en las cartas y guias recomendadas para el examen de los niños. Para relatar los progresos de cada edad mencionada es imposible en un extracto, sin embargo al final del segundo año los progresos hechos en varias actividades pueden ser sintetizados como sigue: 1. El niño puede caminar, correr, trepar y saltar; puede ir hacia atras, hacia los lados, puede usar sus pequeños musculos con considerable habilidad. 2. El niño acepta una gran variedad de comidas y se alimenta el mismo bastante bien. 3. Usualmente duerme toda la noche sin despertarse y a menudo toma una siesta al mediodia. Se habitua a un horario para ir a la cama. 4. Usualmente tiene ya la responsabilidad de sus eliminaciones y el control de su vejiga eliminando durante el dia, algunos accidentes sin embargo pueden ocurrirle. 5. Ha aprendido ya mucho acerca de la conformidad pero todavia no coopera completamente. Piensa y su atencion se va haciendo mas organizada aunque todavia es transitoria.

115½ First Ave. S.W.

CHILDHOOD BEHAVIOR SEQUELAE OF ASPHYXIA IN INFANCY

With Special Reference to Pertussis and Asphyxia Neonatorum

By GEORGE B. ROSENFELD, M.D., AND CHARLES BRADLEY, M.D.
New York, N.Y., and Portland, Ore.

FOR some years members of the staff of the Emma Pendleton Bradley Home have been impressed by a fairly uniform overt behavior pattern in maladjusted children who have experienced asphyxiant illness in infancy. Six cardinal behavior characteristics make up this syndrome and may be listed as follows: 1. Unpredictable variability in mood; 2. Hypermotility; 3. Impulsiveness; 4. Short attention span; 5. Fluctuant ability to recall material previously learned; and 6. Conspicuous difficulty with arithmetic in school.

Asphyxiant illness most frequent in the past history of children showing these behavior characteristics has included pertussis, pneumonia and asphyxia neonatorum.

Since the literature contains no reference to this particular behavior syndrome or its association with asphyxia as a common etiologic factor, the present study was undertaken to test the validity of what has so far been merely a clinical impression.

MATERIAL AND METHODS

The data used in this investigation were obtained by surveying the hospital records of 673 children admitted especially for behavior disorders to the Emma Pendleton Bradley Home, a children's psychiatric hospital, over a 16 year period. Selected for special scrutiny were the records of all children known to have suffered from pertussis and those for whom there was a definite history of difficult resuscitation after birth. The primary object of this study was to correlate the effects of asphyxia in infancy with later childhood behavior. Since pertussis and asphyxia neonatorum have little in common aside from the asphyxia that may characterize each, any similarity in subsequent effects of the two disorders is presumably the result of this common factor. As a control group for comparison with the foregoing, 100 children in whose past records there were no episodes of asphyxiant illness were selected. Although histories of other illnesses producing anoxia such as pneumonia, tracheo-bronchitis and bronchial asthma merit consideration, adequate data relating to them were not available for inclusion here.

The entire group of patients ranged in age from approximately 3 to nearly 13 years at the time of their admission. Their records covered their study and treatment as inpatients for periods ranging from one month to upwards of two years in the hospital. Since only children of average or superior intelligence are eligible for admission to this particular institution, this series contains no mentally retarded children. All had been admitted for psychiatric reasons sufficient in severity to warrant hospitalization but varying widely in type and presenting symptoms. Although the syndrome itself was occasionally the immediate cause for referral, more serious problems of adjustment ap-

---

From the Emma Pendleton Bradley Home, E. Providence, R.I.

Portions of this study were financed by a grant from the Committee for Research in Dementia Praecox founded by the Supreme Council, 33rd degree, Northern Masonic Jurisdiction, U.S.A.

(Received for publication April 8, 1948.)

parently secondary to its presence were more frequent reasons, except in the control group.

Since this study deals only with resident patients, it is obvious that all observations and comparisons were made under fairly uniform conditions. The children were all under the direct surveillance of physicians, nurses and teachers trained and experienced in dealing with children's problems. Their running notes, especially oriented toward the accurate recording of objective behavior data, were incorporated in the hospital records which are the source of this material. The children themselves quite apart from any specific treatment enjoyed a full life of childhood activities and schooling suited to their age and development. They were relatively free both from the usual deprivations of institutional or hospital atmosphere on the one hand and the distractions and variations of life at home and in the community on the other. This setting has been adequately described elsewhere.[1,2]

Material directly related to the six cardinal behavior traits mentioned above is based on specifically recorded observations of the following sorts:

1. *Unpredictable variability in mood.* This term is used to accentuate change in disposition rather than to imply the direction of change. The term "unpredictable" indicates that no observable precipitating cause for these changes was apparent. This type of behavior is what the mother describes when she says, "Some days my boy is just fine and other days I can tell when he gets up in the morning that we're in for a bad time and I can't understand why." The teacher may similarly report, "Sometimes he quarrels with everyone and then all of a sudden, for no reason at all, he's just fine for the rest of the morning." In the hospital records examples of this variability were found in the running notes of nurses and recreation workers and in the comments by the psychologist on children's performance on certain tests.

2. *Hypermotility* was chosen as a term to indicate greater motor activity than is evident in other children of comparable age and physical status. It is frequently most evident as restlessness, darting about, or running rather than walking. The accent is on motion. This characteristic like variability was best illustrated in the notes kept by the ward and recreation personnel or in the description by the psychologist of adjustment to various testing situations.

3. *Impulsiveness* is a term employed to describe a child's quick, often heedless, making of decisions, responding to or resisting suggestions, or reacting to situations about him. These are always to be compared with the usual reactions of other children of similar age and development and living in the same environment. This is the type of behavior implied by the parent who reports, "My child always acts first and thinks afterwards." Like the two preceding traits, it was a matter of record in the nursing notes or in the psychologic reports.

4. *Short attention span* refers to the length of time a child continuously applies himself to a particular interest or task. Due regard must always be held for his own developmental level and the nature of the focus of his attention. For the purposes of this study, comments on this factor appeared in the school teacher's reports, in the psychologist's observations, in the notes by physicians describing the reactions during daily activities, and in the course of psychotherapeutic interviews, and in observations by the recreational director covering sports periods.

5. *Fluctuant ability to recall material previously learned.* This may be a cumbersome phrase but will be readily recognized by any experienced school teacher or clinical psy-

chologist. For the layman it may be most frequently described in terms of "remembering and forgetting." It is often revealed by a parent giving a history by the use of such expressions as, "for a few days he seems to learn everything rapidly, remembering it nicely, and then for a day or so you'd think he had never learned anything about it." Objective evidence of this particular characteristic appeared in notes describing variability in response to specific items in several psychometric tests, particularly the Knox Cube

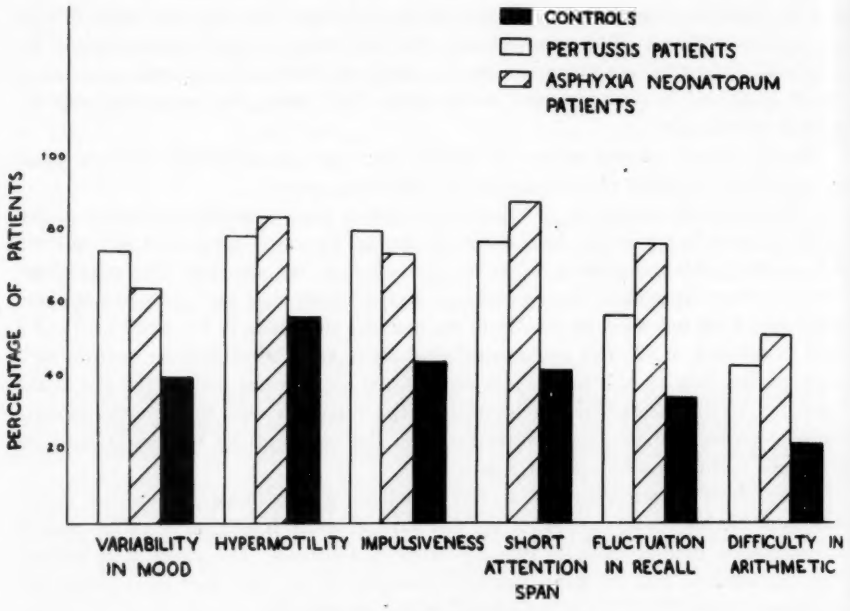


CHART I. Comparative incidence of significant behavior characteristics in 126 children with a history of pertussis during first 3 years of life, 28 children with a history of asphyxia neonatorum, and 100 control children with no history of asphyxiant disease.

Tapping in the Arthur Point Scale, digit repetition, memory of sentences and memory of stories in the Stanford-Binet test, and items on digit symbols and memory for design in the Cornell-Coxe test.

6. *Conspicuous difficulty in arithmetic in school.* This is significant of course only in the light of a child's general intellectual endowment and the extent and quality of his previous school experience. In spite of these limitations, this characteristic was obvious in the children studied from the reports of their rating in various school subjects by the education director using the Metropolitan Achievement Tests. It also appeared in notes covering a child's adjustment to the hospital's school and from comments made by parents on giving a school history at the time of admission.

In considering the results about to be enumerated emphasis is obviously upon such overt behavior as may be capable of objective description and recording. The observations

were made by a trained staff with consistent viewpoints over a number of years. The long-term observation of patients in a uniform setting is of undoubted significance. Reasons for focusing upon a history of pertussis and asphyxia neonatorum to the exclusion of other asphyxiant illness was based upon the availability of adequate data.

Since the group of children with a history of pertussis differed in size from that characterized by a record of asphyxia neonatorum and also from the control group, it was necessary to make comparisons in terms of incidence of traits expressed in percentages of the total in each group. Comparisons were made of the incidence of children showing each

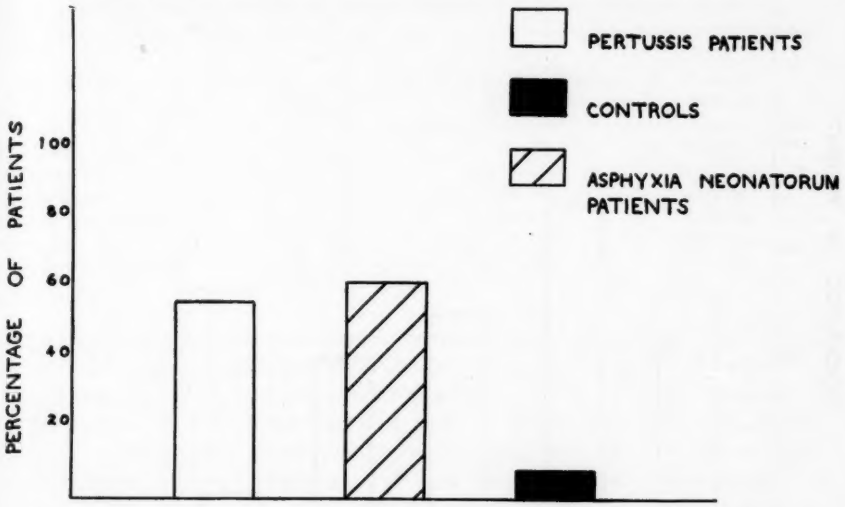


CHART II. Incidence of patients showing 5 or 6 significant behavior characteristics in 126 children with a history of pertussis during first 3 years of life as compared with 28 children having a history of asphyxia neonatorum and 100 children with no history of asphyxiant disease (controls).

individual trait (Chart I) and also of such children as showed at least five of the six traits (Chart II). To determine in the pertussis group the possible relation of the time of illness to subsequent behavior, the children were divided into sub-groups dependent upon the age at which pertussis occurred and the percentages of those showing at least five traits in each group were compared (Chart III).

OBSERVATIONS

Numbers of children studied. Of the 673 children studied 126 (18.7%) had a history of pertussis occurring sometime in the first three years of life. Twenty-eight children (4.2%) had a history of difficult resuscitation at birth and for these a diagnosis of asphyxia neonatorum seemed justified. The control group of 100 children were also taken from the 673 admitted for behavior disorders, but none of them had experienced asphyxiant illness prior to admission. For none of this group moreover was there a history of convulsive disorder or any clear-cut condition such as head injury, poisoning, etc., such as might be suspected of having damaged the central nervous system.

In addition to the 126 patients with a history of pertussis before three years, an additional 143 had experienced pertussis after the third year but prior to hospital admission. Out of this total group of 269 children who had suffered from pertussis prior to admission were selected the subgroups which provided the material for Chart III based on the age at which pertussis occurred.

Comparative incidence of individual traits. In an attempt to determine whether each of the apparently cardinal traits was more prevalent in children who had experienced asphyxiant illness as compared with the control group, Chart I was prepared from

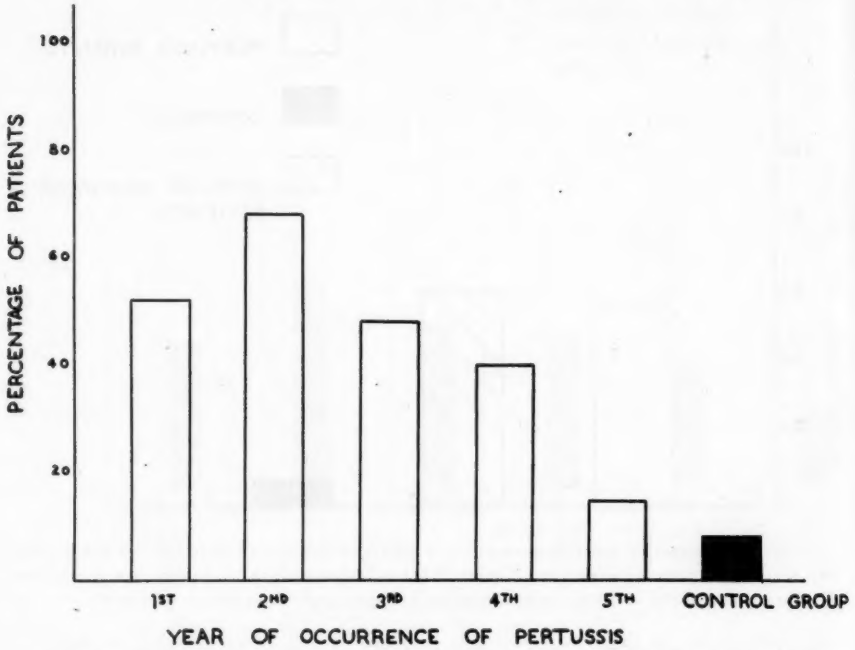


CHART III. Incidence of patients with 5 or 6 significant behavior characteristics grouped by age at which pertussis occurred and compared with incidence in 100 control children with no history of asphyxiant disease.

data presented in Table I. The similarity of columns representing the incidence of each trait in the two groups with history of anoxia, and the relatively low incidence of these same traits in the control group is striking. Speculation as to why some characteristics were numerically more prevalent than others would lead us far afield and it seems wise to limit this study, and any conclusions drawn therefrom, to comparisons between the different groups. The lower prevalence of arithmetic difficulty is somewhat dependent on the age of individual children studied as many of those in lower age range at the time of admission could not be rated on this characteristic. Similarly, the capacities of some of the younger children did not permit their completing all psychometric examinations from which some of these data were obtained.

Since the incidence of each symptom was once and a half to twice as great in the patients

who had suffered anoxia, this portion of the study would appear to validate the original premise that a history of asphyxia in infancy is related to certain behavior deviations in later childhood.

Comparative incidence of entire behavior syndrome. Although the high incidence of individual behavior traits in the asphyxial groups is of interest, each of these characteristics may occur by itself or in other associations in almost any psychiatric disorder. However, a combination of all or most of these particular six traits in one individual seemed to be related to an early history of asphyxia. To test the validity of this impression the material was analyzed to determine how many children in each group were characterized by the presence of five or more behavior traits. In the pertussis group 70 children (55.6%), in the asphyxia neonatorum 17 children (60.5%) and in the control group but seven (7%) exhibited five or more of these symptoms. This is shown graphically in Chart II. The contrast is dramatic, the syndrome being more than eight times as frequent in children with a history of each type of asphyxia as in the control group.

TABLE I

NUMBER AND PERCENTAGES OF CHILDREN SHOWING INDIVIDUAL BEHAVIOR TRAITS

Traits	126 Pertussis Patients	28 Asphyxia Neonatorum Patients	100 Control Patients
Variability in Mood	95 (75.4%)	18 (64.3%)	40 (40%)
Hypermotility	100 (79.7%)	24 (85.7%)	57 (57%)
Impulsiveness	102 (80.9%)	21 (75.0%)	44 (44%)
Short Attention Span	99 (78.6%)	25 (89.3%)	42 (42%)
Fluctuant Recall	72 (57.1%)	22 (78.6%)	35 (35%)
Difficulty in Arithmetic	55 (43.7%)	15 (53.6%)	22 (22%)

TABLE II

PERTUSSIS PATIENTS LISTED ACCORDING TO AGE AT WHICH ILLNESS OCCURRED

Pertussis Occurring In	Number in Group	Number with Characteristic Behavior Syndrome	Percentage with Characteristic Behavior Syndrome
First year	41	22	53.7%
Second year	41	28	68.3%
Third year	44	21	47.7%
Fourth year	37	15	40.5%
Fifth year	26	3	11.5%

Relation of syndrome to age at which pertussis occurred. Clinical experience has indicated that asphyxia from pertussis is seriously significant as a factor in subsequent behavior when it occurs in early life. To test the validity of this hypothesis, the children with a history of pertussis were divided into sub-groups according to the age at which pertussis occurred, and the percentages of those in each group showing five or more symptoms

were compared. The figures by groups up to those who had an attack in the fifth year of life appear in Table II, and the comparative results in terms of percentages are graphically delineated in Chart III. No attempt was made to list the children having pertussis after the fifth year as a significant portion of the total group admitted entered the hospital as early as six years and figures for later groups would appear to be unreliable. The material in Chart III indicates that the importance of asphyxia from pertussis tends to drop off after the infancy period and that figures from later age groups tend to approximate what is obtained in the control children. Apparently pertussis asphyxia is most directly related to subsequent behavior when it occurs in earliest childhood.

General conclusions in terms of cardinal behavior traits. The preceding analyses seem to clearly indicate that a behavior syndrome of the six symptoms under consideration may be noted in the majority of maladjusted children who have suffered from asphyxia at the time of birth or in association with pertussis in the infancy period.

No conclusions, however, are justified from these data as to how frequent is this syndrome in all children who have suffered from these types of asphyxia in infancy, as the present samples came only from a selected group of intelligent children requiring psychiatric hospitalization.

Other findings. Records were carefully reviewed with an eye to noting additional findings of significance in the patients under scrutiny. Seventeen children (13.5%) in the pertussis group and four (14.2%) in the asphyxia neonatorum group had a history of convulsions at some time during childhood.

This is approximately the same frequency that convulsions are known to occur as the result of other conditions producing cerebral trauma, such as head injury. A behavior syndrome similar to if not identical with that under discussion has been mentioned elsewhere as frequently accompanying convulsive disorders.[3] However, in the present series the incidence of convulsions is so much less than the occurrence of the behavior syndrome that their possible relationships in certain individual cases here need not seriously interfere with our conclusions.

As mentioned previously, this is not an unselected group as far as intelligence is concerned, since children with frank mental deficiency are not admitted to the Bradley Home. Therefore, the fact that the intelligence quotients of the children studied were all in the normal or superior range (I.Q. 70 to 130+) is not significant. Physical and neurologic examinations, while revealing a variety of minor individual deviations from accepted normal standards, were not remarkable as far as the entire groups were concerned. The same situation was true for clinical laboratory examinations, including hematology, urinalysis, serology, blood chemistry, and bacteriology, all of which were extensively investigated in the majority of cases included in this report.

Electroencephalographic records were secured for most of the children but complete data referable to the group as herein presented are not at present available and therefore do not merit discussion. It may be noted, however, that a number of apparently normal electroencephalographic records were obtained from some of the children whose histories were definitely pathologic, both in terms of severity of asphyxia and the intensity of behavior symptoms.

From a practical clinical viewpoint it may be of interest to note that many parents in giving histories of children who had suffered from asphyxiant illness mentioned that their behavior differed markedly from that of anyone else in the family.

Discussion

If, as seems obvious from the material presented, a history of asphyxiant illness in infancy may in some children be related to certain uniform behavior characteristics in later childhood, the connection between cause and effect may be sought in two general areas. On the one hand the central nervous system, particularly those portions of it which control and direct overt behavior, may have been damaged during periods of relative anoxia. On the other hand the organism as a whole may have reacted emotionally to desperate and terrifying illness in infancy in some way which is reflected in later behavior patterns. At the present time there is considerable tangible evidence that the first of these premises is probably the more important.

Chornyak[4] and Van Liere[5] have extensively reviewed the effect of anoxia on the central nervous system, with particular reference to structure and function. Their discussions, however, refer only by implication to the particular problem with which we are now concerned. Nelson,[6] in reviewing the neurologic sequelae of pertussis in children, suggests that focal damage to the central nervous system is the result of minute hemorrhage, circulatory stasis, or encephalitis. Dologopol,[7] in a later communication, states that lesions in the nervous system produced by pertussis are not a reaction to the infection per se, but to circulatory disturbances. As Chornyak and others have pointed out, interference with efficient cerebral circulation may be an immediate result of anoxemia.

In discussing cerebral damage associated with traumatic birth, Schreiber[8] states that asphyxia is by far the most common direct etiologic agent. He also emphasizes the fact that microscopic lesions within the central nervous system due to anoxia are identical regardless of the factors producing the anoxia. Windle,[9] Smith[10] and Traut[11] review considerable evidence that the fetus and newborn organisms, both animal and human, can actually survive degrees of anoxia that would be fatal in later life. They point out that survival in itself does not guarantee freedom from serious damage to nervous structure. Smith suggests that, "it is perhaps reasonable to speculate whether such resistance to anoxia as occurs in the human fetus and infant may not be something of a mixed blessing; it may diminish or retard the appearance of those danger signals which warn the obstetrician of anoxic crises, and may allow the infant to exist as a damaged individual after an interlude which would have caused the death of an adult organism." The present study offers considerable support to this speculation.

Although there have been several investigations, such as that of Darke,[12] on the effect of asphyxia neonatorum and other insults to the nervous system as related to resulting mental deficiency, they are not directly pertinent to the present study in which mental defectives were not included.

Personality changes and behavior disorders of children from structural brain injury are subjects of an extensive literature recently reviewed by Bender.[13] Post-encephalitic disorders are frequently characterized by the hypermotility and impulsiveness which are components of the syndrome we are discussing. Bender refers to some of the problems of children who have experienced pertussis and pneumonia in early life but suggests cerebral damage due to hemorrhage or inflammatory reaction rather than asphyxia as their cause.

Chornyak[14] has stressed the probable relationship of certain types of psychopathic personality to severe anoxemia in early childhood.

Lurie and Levy[15] emphasize the importance of pertussis occurring in infancy as a cause

of later maladjustment. They attempted to group the sequelae in terms of clinical problems and general psychiatric concepts rather than in the somewhat more elementary behavior patterns with which we are concerned. In a somewhat similar but by no means identical approach, Preston[16] studied the late results of asphyxia neonatorum in children referred for behavior disorders.

In any study of human behavior at the clinical level psychodynamic considerations must not be overlooked. Deviant behavior as a reaction to fear, anxiety or other intense emotional experience related to choking, dyspnea, or the extreme discomfort of paroxysms of coughing is always possible as indicated by Pearson[17] in his psychiatric study of an individual case. However, it is contrary to all clinical experience to anticipate so uniform a group of behavior symptoms as a direct result of subjective experience with anoxia at any particular developmental age. Such sequelae to asphyxia occurring at widely varying intervals during the period of rapid development in infancy would be even more unlikely. The matter is, however, worthy of further study.

The sextet of characteristics herein enumerated are not to be thought of as constituting or necessarily contributing directly to any sort of psychiatric entity of "personality type." While each trait and certainly a configuration of the majority of them within the personality of any individual are deviant from what is socially acceptable, their presence alone will not necessarily bring a child to clinical attention. It seems best to think of them as serious liabilities and handicaps which make social adjustment more difficult than would be the case if they were not present. Many children react to such severe handicaps in perverse ways resulting in secondary, though often more conspicuous problems such as behavior disorders, neuroses, or delinquency. This is particularly true if their other personal assets are limited and the attitudes of parents and teachers are unfavorable.

Obviously all children who have experienced asphyxia in infancy do not show these six deviant behavior characteristics later. Possibly the degree of asphyxia or the resiliency of individual structures may influence such results. Moreover, there are undoubtedly many children who differ from their siblings by the presence of variability, impulsiveness, etc. to minor degrees which do not seriously militate against their total adjustment to life situations. However, when a child does come to clinical attention and does possess most of the cardinal traits which his history indicates are presumably related to antecedent asphyxiant illness, the clinician may be reasonably sure that he is dealing with behavior somewhat conditioned by a disordered function of the central nervous system. Treatment for the child and guidance for his parents and teachers may then be planned accordingly.

The prevention of future personality problems is not an exclusive obligation of the psychiatrist, the child guidance clinic, or a mental hygiene program. The present investigation indicates that every physician who deals with mothers and infants may have to share direct medical responsibility for certain children's behavior difficulties. Asphyxia in infancy must not only be treated, it must be prevented. Prophylaxis must include early effectual immunization wherever practical for infectious asphyxiant diseases, such as pertussis. It must also include judicious care of the pregnant mother and conscientious management of her delivery, particularly in regard to the use of narcotic, sedative or anaesthetic drugs which may retard fetal respiration. The newborn infant must be assured of prompt, adequate and sustained oxygen supply. In the treatment of infants suffering from disorders associated with anoxemia every effort must be made

to secure and maintain efficient continued oxygenation of the entire organism. Mere survival, even in the absence of immediate conspicuous complications, is not in itself indicative of complete therapeutic success. Only long-term, follow-up studies, with due consideration for personality factors, can vouchsafe this.

Summary

On the basis of an analysis of the records of 673 children referred for in-patient psychiatric treatment, the majority of those having a history of pertussis in infancy, or asphyxia neonatorum, showed a characteristic behavior syndrome.

The behavior syndrome consisted of the six following traits: Unpredictable variability in mood, hypermotility, impulsiveness, short attention span, fluctuant ability to recall material previously learned, and conspicuous difficulty with arithmetic in school.

Each of these behavior traits occurred from once and a half to twice as frequently in patients with a history of asphyxia in infancy as in a control group.

The syndrome, consisting of at least five of the six traits, occurred more than eight times as frequently in the patients with a history of asphyxia as in a control group.

The syndrome occurred significantly more frequently in children with a history of pertussis when the illness occurred in the first three years of life rather than later.

Since this behavior syndrome presents a serious handicap to successful social adjustment in later childhood, strenuous therapeutic efforts should be made toward eliminating asphyxia as a complication of illness in infancy.

Acknowledgements

The authors are indebted to Dr. John Chornyak whose suggestions initiated this study and to Dr. Gertrude L. Muller who compiled much of the original material.

References

1. Bradley, C., Pioneer hospital for children's behavior disorders, Mod. Hosp. **50**:68, 1938.
2. Bradley, C., Education in children's psychiatric hospital, Nerv. Child. **3**:327, 1944.
3. Bradley, C., Management of convulsive child, Rhode Island M. J., **29**:823, 1946.
4. Chornyak, J., Structural Changes produced in the Human Brain by Oxygen Deprivation (anoxemia) and their Pathogenesis, Edwards Bros. Inc., Ann Arbor, Mich., 1938.
5. Van Liere, E. J., Anoxia: Its Effect on the Body, Univ. of Chicago Press, Chicago, 1942.
6. Nelson, R. L., Neurological complications of whooping cough; review of literature with reports of 2 cases of pertussis encephalitis, J. Pediat. **14**:39, 1939.
7. Dologopol, V. B., Changes in brain in pertussis with convulsions, Arch. Neurol. & Psychiat. **46**:477, 1941.
8. Schreiber, F., Neurologic sequelae of paranatal asphyxia, J. Pediat. **16**:297, 1940.
9. Windle, W., Physiology of the Fetus: Origin and Extent of Function in Prenatal Life, W. B. Saunders Co., Philadelphia, 1940, p. 169.
10. Smith, C. A., Physiology of Newborn Infant, Charles C Thomas, Springfield, Ill., 1945, p. 35.
11. Traut, H. F., Hypoxemia of fetus, West. J. Surg. **54**:379, 1946.
12. Darke, R. A., Late effects of severe asphyxia neonatorum, J. Pediat. **24**:158, 1944.
13. Bender, L., Organic Brain Conditions Producing Behavior Disturbances, In Lewis N. D. C., and Pacella, B. L., Modern Trends in Child Psychiatry, International Universities Press, New York, 1945, p. 155.
14. Chornyak, J., Some remarks on diagnosis of psychopathic delinquent, Am. J. Psychiat. **97**:1326, 1941.
15. Lurie, L. A., and Levy, S., Personality changes and behavior disorders of children following pertussis, J.A.M.A. **120**:890, 1942.

16. Preston, Mary I., Late behavioral aspects found in cases of prenatal, natal, and postnatal anoxia, J. Pediat. **26**:353, 1945.
17. Pearson, G. H. J., Psychic effect of pertussis, Nerv. Child. **5**:316, 1946.

SPANISH ABSTRACT

Secuelas de la Asfixia en la Infancia Relacionadas con la Conducta o Comportamiento del Menor

Un analisis de las historia de 673 niños referidos al departamento de psiquiatria, demuestra que la mayoria de ellos tienen en su historia asfixia neonatorum o tosferina en los primeros tiempos de la vida, mostrando mas tarde variados sindromes de conducta.

El sindrome de conducta comprende las seis cuestiones siguientes: variabilidad en los modos, hipermotilidad, impulsividad, limitacion en la atencion, fluctuacion en la habilidad para recordar materias previamente aprendidas y marcada dificultad para la aritmetica en las escuela.

Cada uno de estos problemas de conducta ocurren de 1.5 a 2 veces en el orden de frecuencia en relacion con los pacientes que marcan asfixia en su historia dentro del grupo controlado.

El sindrome constituido a lo menos por 5 o 6 de las cuestiones señaladas ocurre mas de 8 veces en el orden de frecuencia en relacion con los pacientes que marcan asfixia en su historia dentro del grupo controlado.

El sindrome ocurrio de una manera extraordinariamente frecuente sobre todo en los niños con historia de tosferina siempre que esta tuvo lugar en los 3 primeros años de la vida.

El sindrome de conducta representa un serio complejo para el exito social y el posterior ajuste en la infancia y grandes esfuerzos terapeuticos se recomiendan para eliminar los sindromes asficticos como responsables de estas complicaciones en la infancia.

239 E. 58th St., New York
University of Oregon Medical School, Portland

ACCIDENTAL INJURIES IN EPILEPTIC CHILDREN

MILTON R. AISENSON, M.D.
Brooklyn, N.Y.

THE athletic privileges of convulsive children are often restricted because of fear of injury. Search of the literature indicates that there are no published data to support this attitude. The present report compares the injuries to convulsive and non-convulsive children encountered in over 16 years' experience at a children's psychiatric hospital.

MATERIAL

The Emma Pendleton Bradley Home has been fully described in previous publications.[1, 2] Approximately 50 children are residential patients for neurologic or psychiatric disorders. For the most part, they are 4 to 13 years old, of average or superior intelligence, and fully ambulatory. The average stay is 9 to 12 months. The grounds and the general atmosphere suggest a school, rather than a hospital. All children participate in a full program of activities, including about three hours a day in organized athletics, suitable to the weather and to the age of the child, all under the supervision of qualified instructors. In addition, spontaneous activities, such as climbing trees, are encouraged to the limit of the child's confidence.

The records of the 960 patients discharged since the hospital opened in 1931 were reviewed. All patients had an extensive history, repeated physical examinations, many laboratory studies, and detailed progress notes. The diagnosis of convulsive disorder was made in 210 patients; it does not include children who may have had isolated convulsions in infancy, e.g., with fever, but no further manifestations.

The remaining 750 patients comprise the non-convulsive group. Most of these were admitted for behavior problems and were physically normal, except for minor pathology or intercurrent illnesses. Schizophrenia and various neurologic syndromes of childhood comprise the bulk of the remainder.

Age and sex distribution, length of stay, and daily program of the two groups were sufficiently similar to consider this a controlled study.

In both groups of children minor injuries occurred frequently. "Sprains," abrasions, contusions, and lacerations are not included in this study, since they were often not reported and are difficult to evaluate objectively; except for an occasional superficial infection, these healed uneventfully. Fractures and dislocations were confirmed by X-ray. Eye injuries were diagnosed by ophthalmologic consultants. No other accidental injuries were encountered.

RESULTS

The 28 children who were injured during their hospital stay are listed in Table I. Among 750 non-convulsive children, there were 22 who were injured, an incidence of 2.9%. Of these, 18 were fractures, 2 dislocations, and 2 eye injuries. One patient (No. 8) was hospitalized for six months. No. 22 lost the sight of one eye. All others recovered without residual disability. The injured children were all behavior problems, but es-

---

From the Emma Pendleton Bradley Home, East Providence, R.I.
(Received for publication April 9, 1948.)

sentially normal on physical examination. It should be further noted that none of these 22 children had even an isolated convulsive episode, either before or during their hospital stay, although such a history was not infrequent in the 750 non-convulsive children.

Six of the 210 convulsive children were injured during their hospital stay, an incidence

TABLE I

ACCIDENTAL INJURIES IN 960 PATIENTS (APRIL 9, 1931 TO DECEMBER 31, 1947)

	No.	Age in years	Sex	Site of Injury	Circumstances
22 IN 750 NON-CONVULSIVE CHILDREN (2.9%)	*FRACTURES*				
	1	13	M	Tooth	Playing baseball; hit by another child
	2	13	M	a) Right radius and ulna	High jumping; landed on wrist
				b) Right radius and ulna	Playing football; lost balance
	3	13	M	Phalanx, 4th finger, left	Playing outdoors
	4	8	F	Right radius and ulna	Coasting downhill on sled
	5	8	M	Right tibia	Playing outdoors; tripped while being chased
	6	10	M	Right radius	Fell while jumping
	7	10	M	Right tibia and fibula	Jumped off rock
	8	11	M	Left temporal, mandible	Fell 20 feet from tree
	9	13	M	Right radius and ulna	Fell from tree while climbing
	10	10	M	Right radius and ulna	Fell from tree
	11	12	M	Left radius	Fell from tree while swinging
	12	13	F	Phalanx, 2nd finger, right	"Rough-housing" with another child
	13	8	M	Left tibia and fibula	Jumped off wall while stealing apples
	14	10	M	Left 2nd metacarpal	Struck on hand by rock
	15	10	F	Phalanx, 1st toe, right	Rock rolled across foot
	16	9	F	Left tibia	Tripped while walking
	17	13	M	Left radius	Fell on wrist
	18	9	F	Left tibia	Another child fell from tree; landed on her
	DISLOCATIONS				
	19	12	F	Right elbow	Fell 6 feet from log bridge
	20	12	M	a) Right elbow	Boxing
				b) Right elbow	Collision with another boy during play
	OTHERS				
	21	12	M	Left eye (hyphemia)	Hit in eye by baseball
	22	12	M	Right eye (hemorrhage)	Hit in eye by basketball
6 IN 210 CONVULSIVE CHILDREN (2.8%)	*FRACTURES*				
	23	11	M	a) Right 4th metacarpal	Playing soccer
				b) Right 1st metacarpal	Fighting with another boy
	24	8	F	Right astragalus	Fell while climbing stairs
	25	10	M	Left humerus	Fell off wall while going to pond
	26	11	M	Right radius	Fell from tree while playing
	27	13	M	Right cuneiform	Tripped while kicking object on ground
	28	11	F	Right radius	Tripped over root
	OTHERS				
	None				

of 2.8%. These were all fractures. There were no deaths or residual disability due to accidental injury. Discussion of etiologic diagnosis and treatment of these children is not contributory to this study. In two children (No. 24 and 28), seizures occurred frequently, up to six or seven a day; No. 26 had one during a year at the hospital.

Although about one-fourth of the patients at any given time were less than eight years old, none of these was injured. The majority of injured children were boys, similar to the sex distribution in the hospital population. An extremity was the most frequent site of injury. Injuries occurred in organized games, in casual play, by fall from heights, and in such innocent ways as tripping while walking.

Discussion

In over 16 years of observation at a children's psychiatric hospital the accident rates in convulsive and non-convulsive children were similar, 2.8% in 210 convulsive children and 2.9% in 750 non-convulsive children. No other reports are available for comparison. These figures are higher than the National Safety Council's report[3] of accidents in 762,369 school children in nine months of 1946 and 1947. In these children, there were 15,712 accidents that either required a doctor's attention or caused at least a half day's absence, an incidence of 2.1% of the total.

Most convulsive patients admitted to the Emma Pendleton Bradley Home had been severely limited at home, either because of lack of athletic facilities or an overprotective attitude of the parents. Although in 36 states convulsive children are admitted to regular classes,[4] their athletic privileges are often limited, as determined by local policy.[5, 6] Price,[6] in a personal communication, states that of 17 summer camps interviewed, 15 refused to accept convulsive children. Fear of injury to the child is a major reason for this attitude. Parents at home, teachers in school, try to "protect" these children by limiting their activities. This is an important cause of maladjustment in childhood and in older life. The child who does not do the same things as other children will have few friends. Motor skills, as well as social adaptability, develop only with experience. The fact that so many convulsive patients are successful in varied occupations confirms the potentialities of this group.

At the Emma Pendleton Bradley Home games and other forms of physical activity are deliberately encouraged as part of the therapeutic program. For example, tree climbing might be considered dangerous, particularly to a child subject to momentary loss of consciousness. Only one convulsive and four non-convulsive children were so injured.

This study is particularly applicable to schools and camps, where activities are under the supervision of qualified adults. Since there is no additional risk of injury, there is no need to limit the convulsive child's participation in supervised physical activities. Many convulsive patients can be completely controlled by available methods of treatment. In selected patients, such as those subject to frequent seizures, climbing activities may be limited. Swimming is an excellent sport, but does require exceptionally close and competent supervision. Protective devices, such as headguards or mats, should be used when available. In order to satisfy school and camp authorities, the parents of the convulsive child should assume responsibility for injuries that might occur as the result of a seizure. The physician can encourage the parents to request athletic privileges for their children and urge schools and camps to make facilities available.

SUMMARY

The records of 960 residential patients engaged in a full athletic program at a children's psychiatric hospital were reviewed in order to compare the incidence of potentially serious injuries in convulsive and non-convulsive children.

Of 210 convulsive children, 2.8% were so injured. Of 750 non-convulsive children, 2.9% were so injured.

Since no extra risk of injury was found in convulsive children, it is suggested that they be allowed full participation in physical education programs in schools and camps.

REFERENCES

1. Bradley, C., Pioneer hospital for children's behavior disorders, Mod. Hosp. **50**:68, 1938.
2. Bradley, C., Treatment of convulsive child in children's psychiatric hospital, Nervous Child. **6**:76, 1947.
3. School Accident Reports, Accident Facts, 1947 Edition, National Safety Council, Chicago, Ill., p. 91.
4. Potter, Mrs. Brooks, Building a Future for the Epileptic Child, American Epilepsy League, Boston, Mass.
5. Good, C., from Epileptic Children, Board of Education, New York, N.Y., 1941. p. 17.
6. Price, J., Personal communication.

SPANISH ABSTRACT

Traumatismos Accidentales en Niños Epilepticos

Los privilegios del atletismo resultan limitados en los niños que sufren de convulsiones por temor a los traumatismos. Esta circunstancia oculta sus actividades motoras y produce naturalmente un mal ajuste social mas adelante en la vida de estos niños.

En un record de 960 pacientes de niños revisado en el Hospital Psiquiatrico se estudia la influencia de un programa athletico bajo la supervision de adultos. Entre 750 niños no convulsivantes hubo 18 fracturas, 2 luxaciones, 2 heridas de los ojos, con un total de 22 traumatismo y una incidencia de 2.9%. Entre 210 niños convulsionantes hubo 6 fracturas, ningun otro traumatismo, con una incidencia de 2.8%. En consecuencia no hubo ningun riesgo extra de traumatismo entre los niños convulsionantes que se les permitio participar en el programa de educacio fisica en campos y escuela.

1048 75th St.

Pediatrics

VOLUME 2 JULY 1948 NUMBER 1

AMERICAN ACADEMY OF PEDIATRICS, INC. PROCEEDINGS AND REPORTS

PEDIATRICS AND ECONOMICS

By WARREN R. SISSON, M.D.

WHETHER we like it or not, we must admit that we are living and working in a period of basic changes in the economic aspects of the practice of medicine.

There was a day when the physician could make his visits on a completely individual basis and charge as much for his services as he considered appropriate. His bills were entirely between himself and his patients.

But today an increasing number of physicians are finding themselves participants in one or another of the many medical care plans which are spreading rapidly throughout the country. A great variety of plans are being developed by public welfare agencies, health departments, non-profit organizations, medical societies, unions, cooperatives and other groups. Under the provisions of these plans the physician must abide by certain regulations directly affecting his practice and the fees he is entitled to collect.

The growth of the Blue Shield plans for voluntary medical care insurance has been phenomenal and is now so rapid that it is impossible to state accurately from day to day the number of their subscribers. A recent estimate indicates that there are 48 plans with more than 7,000,000 subscribers. In fact Blue Shield seems to be on the way to catching up with Blue Cross, which now has some 30,000,000 subscribers.

Other plans are testing different methods of providing service. One of the most notable of these is the Maryland Medical Care Program,[1] which was established by legislation in 1945 providing that the State Department of Health should administer a program of medical services for indigent and medically indigent persons. Under the provisions of this plan county health officers have assumed administrative responsibility for this program of medical services; physicians are paid directly by the State Treasurer in accordance with a fixed fee schedule.

Another plan which merits careful study is the Health Insurance Plan of Greater New York, a non-profit pre-payment medical care insurance program. It provides its

---

Read at the Areal Meeting of the American Academy of Pediatrics, May 1, 1948, Buffalo, N.Y.

From the American Academy of Pediatrics, Study of Child Health Services, John P. Hubbard, M.D., Director, 2346 Massachusetts Avenue, N.W., Washington 8, D.C.

members fairly comprehensive medical and hospital service; the medical care is given by groups of physicians who are remunerated on a capitation basis rather than a fee for service basis.

Furthermore, it is not necessary to remind you that we are confronted with a plan for national health insurance administered by the Federal Government. Under this plan the cost of medical care would be met by an increase in the Social Security tax. This proposal is familiar to you in the Wagner-Murray-Dingell Bill. It has been repeatedly introduced into Congress and has gained strong momentum during recent years despite the fact that it has been, and continues to be, vigorously opposed by organized medicine and other strong groups. It cannot be overlooked nor neglected.

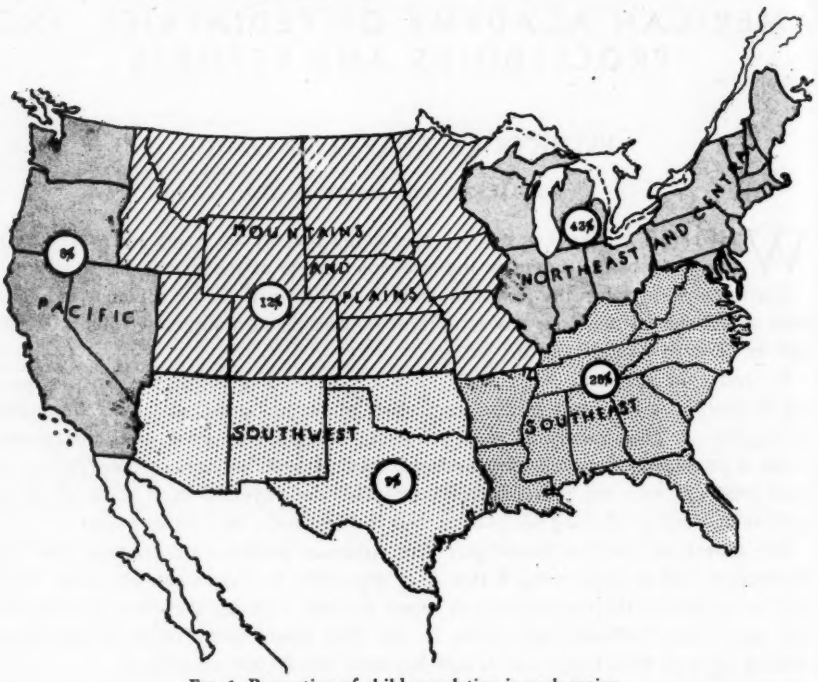


FIG. 1. Proportion of child population in each region.

One of the nation's elder statesmen, one of our foremost economic advisors, has made some very direct statements to the medical profession. After careful study of general medical care for all, Mr. Bernard Baruch, in an address at a dinner sponsored by the Medical Society of the State of New York,[2] said:

"There is no question—the need for medical care exists. There is also no question that this need will have to be met. The problem is how.

"All over the world the masses are stirring for higher living standards. . . . In the matter of adequate medical care, too many doctors have been fighting a rear guard action for too long. I feel I must warn those doctors—time is running against them. The medical profession has justly earned great influence in the community. It can keep that hold only as it moves forward. It will lose that hold if it has nothing but objections to offer, if it has eyes only for what not to do."

Mr. Baruch offered a comprehensive fifteen-point program, and recommended compulsory health insurance for those unable to pay for voluntary insurance plans. The first two of a list of specific proposals which Mr. Baruch offered for the consideration of the medical profession are: "(1) More and better doctors in more places, (2) an immediate complete survey to modernize medical education with greater emphasis on chronic and degenerative diseases, mental hygiene and preventive medicine." Mr. Baruch assumed that sound planning would necessarily have to be based upon factual knowledge of existing health services. He recommends just such a thorough survey as has now been made by the American Academy of Pediatrics.

The Academy's nation-wide Study of Child Health Services is now nearing completion.

TABLE I

ECONOMIC AND HEALTH INDICES

Region	Income per Capita 1944–1946[a] (1)	Infant Mortality Rates per 1,000 Live Births 1941–1945[b] (2)	Percent Live Births Occurring in Hospitals 1945 (3)
Pacific	$1,424	34	97
Northeast and Central	1,321	36	91
Mountain and Plains	1,058	36	87
Southwest	907	54	70
Southeast	753	49	52

[a] Based on income estimates by Sales Management, Vol. 54, 55, and 56, 1945-1947; issue No. 10 of each volume.

[b] Computed by the U. S. Children's Bureau from reports of the National Office of Vital Statistics.

It has disclosed a wealth of facts which can be used as tools for the improvement of child health. For the purposes of this present discussion, I wish to mention only a few of these facts which illustrate the impact of economic factors on the health of children and on the availability of medical services.

In order to compare health services in different parts of the United States, the country has been divided into five geographic regions. These regions with the percentage of child population in each are Northeast and Central (43%), Southeast (28%), Southwest (9%), Mountain and Plains (12%), and Pacific (8%) (Fig. 1). Since this Areal Meeting is concerned particularly with the Northeastern and Central region, a few comparisons have been made to indicate how this section of the country compares with other parts of the country.

The health of a region is related to its wealth (Table I). Where income is high, infant mortality is low, and a high proportion of babies are born in hospitals. Where income is relatively low, the reverse is true. The Northeast and Central region compares favorably with the rest of the country, but does not stand as high in relation to these factors as the Pacific states.

In Table II these five regions have been again listed in the same order according to the rank of per capita income. The number of physicians, general practitioners, and beds in general hospitals for each 1,000 children in each region are given. In the more

TABLE II

AVAILABILITY OF PHYSICIANS IN PRIVATE PRACTICE AND BEDS IN GENERAL HOSPITALS
(Rates per 1,000 children)

Region	All Physicians (1)	General Practitioners (2)	Beds in General Hospitals (3)
Pacific	4.1	2.2	18
Northeast and Central	4.5	2.8	16
Mountain and Plains	2.9	2.0	15
Southwest	1.8	1.2	9
Southeast	1.7	1.2	8

wealthy Pacific and Northeast and Central regions, there are approximately twice as many physicians, twice as many general practitioners, and twice as many hospital beds in relation to child population as in the two southern sections which rank lowest in the economic scale among these five regions.

Furthermore, the children in the more wealthy regions receive more physicians' services than do the children in the poorer regions. Table III shows that children in the Pacific, Northeast and Central regions receive about one and a half times as much care from physicians in home, office, and hospitals, as the children in the Southwest and the Southeast. It is especially significant that in the more wealthy regions where the rate of physicians is higher, the amount of health supervision which is given to children by physicians is much more than in the less wealthy regions of the Southeast and Southwest. In the Pacific states, 31% of the care given to children by general practitioners was for health supervision, and 65% of the care given to children by pediatricians was for health supervision. But in the Southeastern states these proportions were 21 and 49% respectively.

The Northeast and Central region is the major industrial and commercial area of the country. Its wealth has fostered the development of numerous medical facilities and has attracted physicians and others who render health service. It contains half of the medical schools of the country and 61% of all pediatricians in private practice.

TABLE III

PHYSICIANS' VISITS TO CHILDREN ON ONE DAY

Region	Physicians' Visits per 1,000 Children (1)	Percent of Visits Which Were for Well-Children	
		General Practitioners (2)	Pediatricians (3)
Pacific	15	31	65
Northeast and Central	17	31	57
Mountain and Plains	14	29	52
Southwest	10	25	57
Southeast	10	21	49

Yet if we look at the area more closely, sharp differences are revealed in the availability of physicians and hospital beds as well as physicians' services in metropolitan counties in comparison with isolated rural counties. It has previously been reported[3] that, for the purposes of this Study, counties have been classified in five groups according to population and proximity to densely populated areas. These five groups are: greater metropolitan, lesser metropolitan, adjacent, isolated semi-rural, and isolated rural. Table IV shows the distribution of physicians and general hospital beds among these five county groups of the Northeast and Central region. In the greater metropolitan counties, in which the per capita income is more than twice as great as that of isolated rural counties, for every 1,000 children there are three times as many physicians, and five times as many general hospital beds as in the isolated rural counties. It is to be expected that there should be greater concentration of hospital beds and specialists'

TABLE IV

AVAILABILITY OF PHYSICIANS IN PRIVATE PRACTICE AND BEDS IN GENERAL HOSPITALS: NORTHEAST AND CENTRAL REGION
(Rates per 1,000 children)

County Group	All Physicians (1)	General Practitioners (2)	Beds in General Hospitals (3)
Greater Metropolitan	5.8	3.4	19
Lesser Metropolitan	4.1	2.4	16
Adjacent	2.8	2.3	11
Isolated Semi-Rural	2.9	2.3	12
Isolated Rural	1.9	1.9	4

services in metropolitan areas. However, children in isolated rural counties need just as many general practitioners as the same number of children in the metropolitan centers. In fact, it might be argued that in rural areas there is need for a higher rate of general practitioners since distances are greater and there are fewer specialists to share the load with the general practitioner. Yet here it is seen that there are twice as many general practitioners per 1,000 children in the greater metropolitan counties as in the isolated rural counties.

Table V shows that children in isolated counties not only get less care from physicians in private practice than do children in the metropolitan counties, but also the relative amount of health supervision is less. It may be assumed that in the isolated areas physicians are so busy taking care of sick children that the time available for health supervision is correspondingly limited.

These are only a few of the facts which the Study is now revealing. They are sufficient, however, to illustrate clearly the inequalities in the amount of medical care received by children in various sections of the country—inequalities which are closely linked to economic factors. Children in isolated areas are handicapped particularly in specialist care, clinic care, and the highly skilled diagnostic and treatment services—those very services which have been agreed upon as the right of every child.

How are these deficiencies to be remedied?

It is our conviction that before other health measures can be effected, steps should be taken to assure that there are more physicians who are well-trained in the care of children, especially in the remote and rural areas.

This need can be met only by strengthening pediatric education in medical schools and hospitals, for undergraduates and postgraduates, for general practitioners and pediatricians, and by bringing the benefit of this teaching to the child wherever he is.

But at this point, we are confronted with another fundamental fact, the details of which are now available from our Study of pediatric education. Today any attempt to strengthen pediatric education is immediately blocked by the fact that medical schools are finding it increasingly difficult, if not impossible, to maintain even present standards. It must be admitted that financial support for pediatric departments of medical schools is grossly inadequate. Provisional estimates[4] indicate that the funds allocated to the

TABLE V

PHYSICIANS' VISITS TO CHILDREN ON ONE DAY: NORTHEAST AND CENTRAL REGION

County Group	Physicians' Visits per 1,000 Children (1)	Percent of Visits Which Were for Well-Children	
		General Practitioners (2)	Pediatricians (3)
Greater Metropolitan	19	34	59
Lesser Metropolitan	16	29	56
Adjacent	15	28	51
Isolated Semi-Rural	15	26	49
Isolated Rural	11	27	—

pediatric department by the medical schools average $24,000 a year. Additional funds, largely for research, brings the figure to $44,000 a year (Fig. 2). Over a third of the departments work on teaching budgets of less than $10,000 a year; three of these have no regularly allocated funds for teaching.

The Executive Board of the Academy and its Committee for Improvement of Child Health have expressed the opinion that as a result of data from the Study available at this time, the most pressing need is to extend better medical care to children, to support medical schools throughout the country by giving them financial support for pediatric teaching. Such a plan would enable young men and women interested in teaching and clinical research to extend their periods of study. It has been my personal experience as a teacher for a long period of time, that young physicians enhance greatly the teaching of medicine. They are often near the students' age, are more tolerant in understanding the students' problems, and although not endowed with great experience are often better and more accurately informed in newer technics and understanding of growth and development of the child. Financial help to this group is, perhaps, the greatest need. From this group come the teachers of tomorrow. It is to be emphasized that this group is relatively small, for they must be willing to live on limited funds and must be endowed with enthusiasm to set the pegs ahead by their studies as clinical teachers and investigators. If the American Academy of Pediatrics can be instrumental in foster-

ing this group of young pediatricians, giving them an opportunity to carry out their ambitions, and giving their families a reasonable security, in my opinion, the Study will have been worthwhile.

There are also other and important groups of teachers who must have financial support far beyond that ordinarily given by medical schools. I refer to the so-called half-time physicians. This group is undoubtedly smaller than the previous group, but one which is, in my opinion, essential for a well-rounded teaching unit. Physicians in practice have a point of view that is greatly needed by the medical student, for most all students are going to be practitioners.

Men and women in this group will undoubtedly receive less financial support but

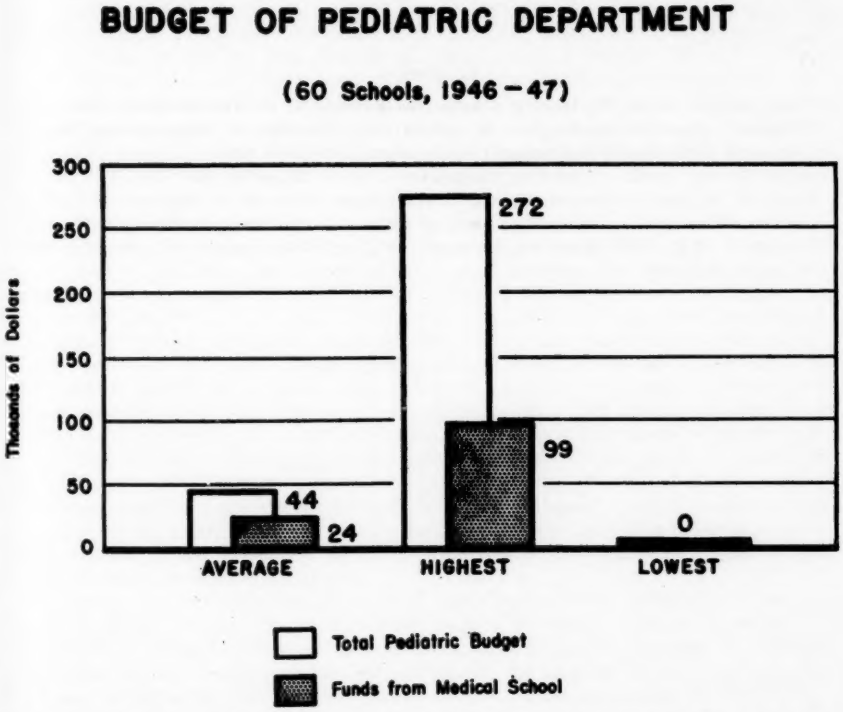


FIG. 2. Budget of Pediatric Department (60 Schools, 1946-47) (From Mitchell, Bain, and Hubbard, Impressions on Pediatric Education, PEDIATRICS, 1:512-518, April 1948).

we must remember that medicine is much more complicated, and teaching requires more time and study than formerly. Here again, the Academy must seek funds for half-time teachers, if better medicine is our goal. By the same token, one must extend financial aid to these groups such as the general practitioners.

One asks immediately from what sources can the funds for pediatricians be secured? The question is not the answer. Some feel that the coffers of private funds have not been exhausted. They must be thoroughly explored. Federal funds are already used for

this purpose, and in the present emergency may have to be sought in increasing amounts. This much is clear: that something must be done, and that medical groups like the Academy must take the lead. If federal funds are utilized, the greatest of care should be taken to retain our complete educational freedom.

By way of summary: socio-economic trends are influencing the practice of medicine to an increasing degree; deficiencies exist in the distribution of physicians and medical care in some areas of the country in comparison with others; the medical profession is being called on to assure that medical care of high quality is available to all persons irrespective of their geographic location. As a first step toward providing better and more evenly distributed medical care to all children, priority must be given to the support of pediatric education in order to provide more physicians well-trained in child care.

References

1. Kline, H. M., Terris, H., Hapney, Cozette, and Kramer, N. A., The Maryland medical care program; report to subcommittee on medical care, Committee on Administrative Practice, American Public Health Association, 1790 Broadway, New York, 1948.
2. Baruch, B. M., speech reprinted in Congressional Record 93:A4573, Nov. 20, 1947.
3. Sisson, W. R., Bain, Katherine, Britten, R. H., Pennell, Maryland Y., Hubbard, J. P., Total volume of medical care for children based on analysis of eight states, PEDIATRICS 1:227, 1948.
4. Mitchell, J. McK., Bain, Katherine, Hubbard, J. P., Impressions on pediatric education, PEDIATRICS 1:512, 1948.

Panel Discussion

A PROGRAM TO DEVELOP AND IMPROVE FACILITIES FOR THE CARE OF NEWBORN INFANTS—FULL TERM AND PREMATURE

By STEWART H. CLIFFORD, M.D., *Chairman,* KATHERINE BAIN, M.D., HENRIETTA HERBOLSHEIMER, M.D., FREDERICK F. TISDALL, M.D., C. ANDERSON ALDRICH, M.D., AND MYRON E. WEGMAN, M.D.

INTRODUCTION

Chairman Stewart H. Clifford, M.D. (From the Boston Lying-in Hospital; the Infants' and Children's Hospital; and the Department of Pediatrics and Obstetrics, Harvard Medical School.): The social trend toward hospitalization for childbirth has gathered amazing momentum in this country. In Massachusetts, for example, 96% of the births now take place in hospitals. This hospital trend has been accompanied by a substantial reduction in the mortality rate for the period from birth to two weeks of life. The Massachusetts death rate from birth to two weeks in the period from 1910 to 1930 was between 35 and 32 deaths per 1000 live births. From 1930 to 1946 there has been a steady decline in the number of such deaths to a death rate of 21 per 1000 live births for the past five years. The latest statistics for the United States as a whole demonstrate a similar improvement—in 1944 the death rate for the first two weeks for the United States was 22 per 1000 live births.

This reduction of 34% in the death rate for babies in the neonatal period between 1930 and 1941 is ample evidence that changing from the home to the hospital for childbirth has reacted to the over-all benefit of the baby. The hospitals of the country deserve a great deal of praise for the results they have accomplished in spite of grave handicaps. They were not prepared for the volume of service they have been called upon to render, and for many reasons it has been impossible to increase the bed capacity sufficiently to meet the load. There has been and there is a real shortage of trained personnel to care for the greatly increased number of patients. Many hospitals are in serious financial difficulties for many reasons and are in no position to engage in elaborate new construction or remodeling—the purchase of adequate equipment is itself a serious problem.

While the over-all picture of hospital care for the newborn has thus far reacted to the advantage of the infant, the present situation is accompanied by certain definite hazards that, uncontrolled, may threaten the infant's welfare. In many hospitals the conditions of crowding, lack of personnel and inadequate equipment make the possibility of introduction and spread of infection in the newborn nursery a constant danger. That many nurseries have actually experienced such outbreaks of infection is evidenced by the literature on epidemics of diarrhea in newborn that have appeared with increasing frequency during the past 15 years.

Many groups and individuals have recognized the great dangers present in many of our newborn nurseries, and much has been done to improve the situation. The Federal Government through the Children's Bureau has been working on this problem for years. It would be impossible to adequately reward those farseeing members of the Children's Bureau for their leadership in improving the lot of the newborn infant—full term and premature. That the newborn nursery situation has not reached the proportion of a national disaster may well be the result of their work. Many state and local health departments have been vividly aware of the problem; and, both on their own initiative and in cooperation with the Children's Bureau, have tried to correct the defects in our present nursery system.

Improvements in the care of the newborn cannot be achieved by regulation or legislation alone. The improvements occur when the doctors and nurses in the individual nurseries learn what constitutes sound nursery theory and voluntarily and enthusiastically put this knowledge into practice. It is surprising how few doctors, struggling with problems in their own nursery, know of the valuable information even now available to them. It is amazing how gratefully they welcome these aids when they are made available.

It is in keeping with the high objectives of the American Academy of Pediatrics that it should

From the Annual Meeting of the American Academy of Pediatrics, Dallas, Tex., December 8, 1947.

assume a leading role in efforts to better the care of the newborn in hospital nurseries. The Academy's Committee on Fetus and Newborn, with the approval of the Executive Board, is sponsoring such a program. Under authorization by the Executive Board, the Committee on Fetus and Newborn wrote each Academy State Chairman requesting the appointment of State Committees on Fetus and Newborn to organize and direct the program within their state. It was emphasized that while there were not enough members of the Academy to carry out the project, the Academy at all levels was offering its good offices as sponsor. All groups and physicians interested in the program are invited and urged to participate. It is a tribute both to the efficiency of the Academy's State Chairmen and to the great interests in the program that within three months of the original request all but one state have appointed Committees on Fetus and Newborn. In all, 56 state committees have been organized, including three from Canada and one from Hawaii.

The Academy Committee on Fetus and Newborn appreciates that its greatest responsibility is to provide the groups and individuals trying to better the care of the newborn with tools and the "know-how" with which to work. We doctors who staff the nurseries for the care of newborn in hospitals are the key personnel in this campaign. Backing us up are the State and National Academy Committees on Fetus and Newborn and over all the knowledge and prestige of the pediatricians of America through the Academy. As individuals we can be fully aware of changes that need to be made in our nurseries to improve newborn care but as individuals we may encounter local difficulties in effecting these improvements. If, on the other hand, we have available standards and recommendations for newborn care representing the collective knowledge of the American Academy of Pediatrics we can review our local situation and make our recommendations backed by the authority and prestige of the Academy.

The Academy Committee on Fetus and Newborn is in the process of compiling a manual of information to assist individuals and groups in their efforts to improve the care of the newborn. The preliminary draft of such a book has been completed and copies have been sent to the officers of the Academy, the State Chairmen, the chairmen of the State Committees on Fetus and Newborn, the members of the Committee on Improvement in Child Health and other individuals and groups in and out of the Academy for their criticism. Over forty detailed reviews of the program have been returned to date with many specific criticisms and concrete suggestions.

The present Panel Discussion serves two functions. First, to acquaint the members of the various State Committees and the individual members of the Academy with a general outline of the program, and to hear from representatives of the Children's Bureau and a State Health Department of the help we can expect to receive from them in carrying out the project. Secondly, to hear from several authorities a critical discussion of proposed standards and recommendations for hospital care of newborn infants—full term and premature. Not only have the speakers been given the Committee's brochure on proposed standards but they have also received copies of the criticisms and suggestions received pertaining to their field.

Functions of the Federal Government in Protecting the Newborn and in Developing and Improving Facilities for the Care of Full-Term and Premature Infants

Katherine Bain, M.D. (From the Federal Security Agency, Social Security Administration, U. S. Children's Bureau.): All modern governments accept as essential the function of collecting vital statistics of their populations. Among a variety of items collected recurrently, a very important pair are births and deaths under one year, for the ratio of infant deaths in the first year to live births serves as a delicate index of the health of a country. Though it is not uncommon to refer to infant mortality rates in the United States around 1900, or even in the last century, the fact is that no reliable figure was available for the country as a whole until 1933. The Bureau of the Census began collecting such data in 1915, admitting a state to the birth registration area when studies showed that 90% of its births were reported. In 1915 the birth registration area comprised only ten states and the District of Columbia. By 1933 all states were in, and national statistics became available. Much of the material issued by the Bureau of the Census is of great value to persons concerned with the planning for the care of infants. The trend in birth rate and the trend in hospitalization for delivery are needed for nursery planning. Infants deaths by cause show up improvements and show also where action is needed. For example, the importance of the premature problem is made

clear when we see that the drop in neonatal death rate has lagged behind the infant mortality rate and that almost one-half of the deaths in this first month are due to prematurity.

With the reorganization of the government in 1946 the Bureau of Vital Statistics was transferred from the Bureau of the Census in the Commerce Department to the U. S. Public Health Service, where it is now called the National Office of Vital Statistics. Regular releases of statistical material are issued and are available to anyone who asks for them.

One other activity of the National Office of Vital Statistics of special interest to physicians might be mentioned. The International List of Causes of Death is revised every ten years and the 1950 revision is now in progress under the sponsorship of the World Health Organization. Dr. Halbert L. Dunn, Chief, National Office of Vital Statistics, represents the United States in this project. The list is being radically revised to include morbidity as well as mortality. For the first time a comprehensive system will be available for the uniform recording of illness as well as death.

Not only is the government concerned with how many babies are born, but it is concerned with the kinds of places they are born in. The Hospital Survey and Construction Act, often known as the Hill-Burton bill, will greatly improve facilities for maternity care and, of course, for newborn care. Under the provisions of the act certain planning and construction requirements have been established which will tend to improve the quality of care in hospitals. The nursery requirements, approved by the Federal Hospital Council, are based on the standards developed by the Children's Bureau several years ago. The translation of the standards into requirements for the hospital construction program resulted in relatively minor changes downward. For example, the maximum number of bassinets allowed in one nursery was placed at 12, but the standard of 8 was recommended. A premature nursery is required only if 25 or more maternity beds are provided, but is recommended for a 16-bed maternity unit.

These nursery requirements have caused considerable discussion because they increase the cost of construction. They are based on the principle that newborn infants should be in small groups, not large nurseries, should have adequate space, not be crowded together; should be protected from unnecessary exposure to other persons; should be separated from sick infants and adults; and should have individual attention.

The U. S. Public Health Service in recommending the establishment of high standards for nursery care had its hand strengthened not only by the Children's Bureau standards already agreed upon and in use, but by a strong supporting statement from the Chairman of the Hospital Committee of the Academy of Pediatrics, which was presented quickly when asked for.

The Federal Hospital Council in accepting the recommendation of the U. S. Public Health Service for these requirements has demonstrated that it believes the benefits of the Hospital Construction Act will be through improving the quality of hospital care, not adding more hospital beds alone.

The activities for newborns just cited are, of course, only minor activities of the Federal agencies involved. The agency of the government with major interest in the health and welfare of children is the Children's Bureau. Its responsibilities in the field of child health may be grouped into two broad categories: first, those authorized under the basic act founding the Bureau such as research and the dissemination of information, and second, those added with the passage of the Social Security Act in 1935, consisting of administration of grants-in-aids to the States for operation of programs to improve child health.

The Congress in the act establishing the Children's Bureau directed it to investigate and report upon all matters relating to child life, including infant mortality, sickness, and a long list of other problems. The Congress accompanied this broad mandate with an appropriation of $26,000 which, back in 1912, provided for a staff of 15 people. Miss Julia Lathrop, the first Chief of the Children's Bureau, very wisely decided to focus this small crew on one segment of the enormous task. Infant mortality was given priority. During the first years of its existence the Children's Bureau concentrated on infant mortality, carrying out field studies in eight cities, collecting data on the social and economic factors which contributed to the very high infant death rate.

A succession of studies dealing with problems of the newborn period has followed these early basic investigations. For example, a study of the centers of ossification in newborn infants was carried out in Baltimore in 1938-39. The very great interest of Dr. Ethel C. Dunham in prematurity led to several cooperative studies in this field. Some of the work of Gordon and Levine and some of that

reported by Dr. Powers at this meeting was financed from the Children's Bureau. Though the Bureau has no money for grants for research and a very small budget for its research staff, it has maintained a great interest in research, has sought to stimulate research, and, to a limited extent, has served as a medium for dissemination of research information.

Both professional and lay persons have turned to the Bureau from time to time for assistance in defining criteria of good child care. The Bureau has considered it one of its major responsibilities to meet such requests through investigation, review of the literature, visits to good institutions, consultation with specialists, and finally, synthesis of data and expert opinion. The standard of care which emerges from such a procedure is put into shape and form by the Children's Bureau staff, reviewed by a wide variety of knowledgeable people, and finally passed on by an advisory committee. This committee has served the Bureau in the capacity of reviewer of publications since 1919. It consists of a representative appointed by each of the four major medical groups in this country who are concerned with child health—the Academy, the Pediatric Section of the American Medical Association, the American Pediatric Society, and the old American Child Health Association. When the "standard" finally emerges from this process, it represents not the opinion of a particular staff member of the Children's Bureau, nor of a particular medical school, a group of physicians, or an individual, but the consensus of the best thought that can be assembled across the country. Standards developed by the Bureau which are in much demand are "Standards and Recommendations for Maternity Care in Hospitals" and "Standards and Recommendations for Hospital Care for Newborn Infants," including prematures.

Hospital administrators, medical directors, or staff have used these standards as goals towards which to plan. State health departments have found them useful in setting up codes for hospital licensing geared down, of course, to meet what is practicable locally. Within the last few years many states have developed hospital licensing, placing responsibility in health departments. Twenty-four now have such laws.

Work is in process in the Children's Bureau on two more sets of standards—standards for pediatric units in general hospitals, and convalescent-care standards. Standards for milk-room layout and procedures are being worked out by a committee of the American Hospital Association, of which one of the Bureau's staff is a member. The committee includes persons who have been most active in research in methods of formula preparation. We hope that the committee will produce a statement which can be accepted by the Children's Bureau as representing the current evidence and opinion on the best methods of formula preparation in hospitals.

With the passage of the Social Security Act in 1935 the Children's Bureau was given new responsibility—the administration of grants-in-aid to states for maternal and child health, care of crippled children, and child welfare. The maternal and child-health funds available for grants to states were $5,820,000 for some years, but in 1946 were increased to $11,000,000. Because many of you are or will be involved in state health department programs using these funds, it seems desirable to take a few moments to explain their administration. Half the money—Fund A—is allocated to states on a formula which provides a flat payment to each state and territory of $35,000, plus an additional amount based on number of live births in the state. States with large populations, as California, New York, and Illinois, which are also the rich states, get large sums. This money must be matched dollar for dollar from state funds. The other half of the appropriation—Fund B—is not matched and is allocated on a formula which is designed to get more of this money into poorer states that need it most. In order to receive its share of the funds a state must submit a plan outlining its program for the coming year and indicating how it will meet certain requirements of the act, such as providing for efficient administration, extending existing services, etc. Programs are as varied as states are numerous. One state expends a sizable proportion of its maternal and child-health funds on a dental program; another spends none in this activity. One state may put great emphasis on a premature program or home-delivery nursing service, while another puts its emphasis on health services for the school age group. The pattern of activity within the state is usually determined by the major needs of mothers and children within the State as revealed in staff studies, or as emphasized by public interest and demand.

When the appropriation was doubled last year the Children's Bureau, acting on the advice of its advisory committee, set aside $1,500,000 to be used for special projects in two fields: the development of training centers for professional personnel in fields related to maternal and child health, and demonstration programs of services to mothers and children including medical and hospital

care as needed. Several states have inaugurated new premature programs, including a training center in premature care, under this provision for special projects. The funds set aside for special projects are completely taken up by now, so that development of new premature programs in the immediate future is dependent on state or local funds, or the Federal funds allotted by formula to the state.

Premature programs financed from maternal and child-health funds are not new. Some states have budgeted funds for this purpose for years. For the fiscal year 1946, 39 state plans indicated some activity in relation to premature infants and five additional states described services proposed for 1947. The services provided by the states vary widely, ranging from postgraduate training for a few hospital nurses, or a loan of incubators to certain hospitals, to an extensive State-wide program of hospitalization and aftercare of premature infants. State plans for the current year show seven states with premature centers now in operation and six more in the process of starting. Most of the states concentrate on one, two, or three good centers to which prematures are brought by ambulance.

Some, but not all, of the states have set up their centers in connection with medical schools and university schools of nursing. These then serve as centers for training personnel. Most of the programs have a pediatrician in charge. Several have advisory committees. For example, in Hawaii all the pediatricians in Honolulu are on the committee, together with representatives from other professional groups.

It is not possible to state how much Federal money is going into premature programs. A state budgets, for example, so much for training which includes persons on the rheumatic fever as well as premature program, or so much for hospital care which might include delivery service for mothers also. Identifiable amounts budgeted for premature programs range from a few hundred dollars to $75,000 for a large program that includes a training center and hospitalization on a large scale. The States of Maryland, Louisiana, Colorado, Illinois, Massachusetts, and Hawaii have developed or are developing sizable programs of care for premature infants.

As you can see, premature programs are going concerns in a number of states and are incipient in others. They need the assistance and backing of the pediatricians in the state. One of the first acts of the newly appointed Academy Committees on the Fetus and the Newborn in the states should be to find out from the state maternal and child-health director what the state program is and offer their services in an advisory capacity. In some states the program must remain simple, for there are neither personnel nor adequate hospital facilities to expand it. Prematures continue to be born in such states, however, and need care just as much as those arriving in more fortunate medical centers. Some provision for care can be made if ingenuity is used. Often the first step is postgraduate training at a premature center in another state for a doctor, a few nurses, and a medical social worker. Assistance from Academy members in evaluating what can be done in a state and support in the doing would be welcomed by all health department personnel concerned with the improvement of child health.

Suggestions for participation of Academy members in state programs for improving newborn and premature care:

1. Participation in hospital planning for the state.
2. Support and interpretation of nursery requirements for participation in funds under the Hospital Construction Act.
3. Support of adequate hospital licensing laws administered by the state health agency. Support of a program of consultative service to hospitals by the state agency to accompany licensing. Assistance in the development of recommended standards for hospitals by the state agency. Participation in developing the code for licensing.
4. Service on state health department advisory committees concerned with nursery and newborn care.
5. Service as consultants or staff members in premature-care programs.
6. Assistance in training programs for doctors, nurses, and social workers in premature programs.

The Function of State and Local Health Departments in Protecting the Newborn and in Developing and Improving Facilities for the Care of Full-Term and Premature Infants

Henrietta Herbolsheimer, M.D. (From the Division of Hospital Construction and Services; formerly Chief of the Division of Maternal and Child Health for the State of Illinois): From the public health point of view the newborn infant is only one component, albeit an important one, of

a community, the health of which is dependent upon many factors in the environment. Responsibility for some of these factors, but by no means all, has been assigned to official public health agencies. To understand the functions of state and local health departments in diminishing the risks of the newborn, it is therefore important to have a general idea of the scope of public health activities. It is also important to appreciate that health department functions vary in accordance with area health problems and are subject to the limitations of size of unit, its operational budget, and the amount of local interest and cooperation that can be aroused in the improvement of community health.

The smallest of the official health units is the rural county or multiple country health department which should contain a professional staff of a public health physician, a sanitary engineer, a health educator and public health nurses, the latter in the ratio of one to five thousand population. The basic functions of local health units include health education, sanitary control of milk and water supply and sewage disposal, vital statistics, public health laboratory and maternal and child health services. In the more populous counties and metropolitan areas, where the call for public health service is greater, the basic functions may be carried on in separate divisions under full complement of staffs trained in the specialties and the science of public health.

On the state level, departments of public health have long-standing statutory powers and duties in the six basic fields enumerated and, in addition, have special responsibilities in keeping informed on the work of local health agencies throughout the state and in assisting them in the administration of health laws. Insofar as possible, the statutory responsibilities of the state health departments are delegated to the local units. Specialized and highly technical or recently acquired responsibilities, are, however, more difficult to delegate to the primary communities because it is impractical for the smaller health units to acquire the specialized personnel, the cost is excessive, or the program details too nebulous. Such is the case with the more recently acquired state health department powers and duties in the field of hospital licensure.

Although health department responsibilities are defined in the pungent legal terms "powers and duties," in actual practice they have come to be interpreted as outlines for educational and persuasional programs to apply the scientific principles which relate to community health. Despite the statutory foundations of health departments activities, the administrative intent is to avoid "due process of the law" and to fulfill the assigned responsibilities through the more pleasant and more effective methods of consultation, conference and cooperation.

In the solution of the remaining challenges of the first month of life there appears to be ample opportunity for use of these methods in extending the application of what is known and in planning a course of action to increase our knowledge. In his discussion of the tremendous improvement in the infant mortality rate, Raymond Pearl* says: "The easy part of the conflict has happened and is in the past. To continue the good fight with the same relative measure of success, one presumably needs to know the pattern of the casual nexus which controls and determines the rate of infant mortality."

Improving the lot of the newborn, is, however, more than a matter of preventing deaths; it includes the prevention of illness and injury and the promotion of physical and emotional health. This is a large task in which the proposed program of the Committee on Fetus and Newborn offers a sound beginning. How, precisely, can state and local health departments contribute toward and cooperate in diminishing the risks of the newborn?

The first thing they might do is to assure the availability of basic public health services to all of the people by stimulating interest in local health units in the one third of the counties of our country that today lack such service. Inasmuch as there is close correlation between infant mortality and the health of the community, the current deficiency in local health services has real bearing on the proposed program of the Academy. Furthermore, areas which lack the administrative framework of personnel, policies, and budget for general health services, are extremely unlikely to develop and maintain a specialized health program for newborn infants.

The actual creation and maintenance of local health units is a matter for local decision. The state health departments have, nevertheless, a proper function in stimulating interest in local services and in assisting established units administratively and financially to provide vital statistics, laboratory

* Pearl, R., Introduction to Medical Biometry and Statistics, W. B. Saunders Co., Philadelphia, 1940, p. 188.

service, communicable disease control, health education, sanitation, public health nursing and maternal and child health services.

Second, state health departments may focus special attention on the newborn through hospital licensure activities. For many years most states have had some kind of control over maternity hospitals, and during the past eight years about a dozen states have been attempting to enforce nursery standards similar to those defined in U.S.C.B. Publication No. 292.* Since the enactment of the Hospital Survey and Construction legislation of 1946, all states must have licensure laws to govern standards of operation in those hospitals which obtain Federal grants-in-aid for construction.

Twenty-four states already have full authority to inspect and license hospitals on the basis of standards established in each state. For the most part this authority has been placed by statute in the State Department of Public Health. This is in conformity with the wishes of the American Hospital Association and the ideas of the Council on State Governments. With regard to the writing of standards, it should be emphasized that health departments seldom, if ever, make up the regulations governing licensure. Instead, it is their practice to compile the standards from the literature of non-official standardizing bodies such as the American College of Surgeons, from the publications of the U. S. Children's Bureau, the U. S. Public Health Service, and from experience locally and elsewhere. It is also customary for the state agencies to submit the proposed regulations to medical, hospital, nursing and related bodies for criticism before the requirements are put into effect. The writing of regulations which are clear, flexible, practicable, and sound is a time-consuming and arduous task.

Aside from the work of reviewing the literature, arranging conferences, editing and re-editing the material, the job of writing standards is made particularly harassing by the lack of scientific evidence in support of many of the time honored requirements for safe operation of hospitals. Partly because there has been a considerable experience with licensure of maternity departments and partly because there is a constant fear of epidemic diseases breaking out in the post-partum wards and nurseries, the body of specifications governing facilities and hospital practices in these two areas of institutions is tremendous. Like laws that get on the book, practices, innocently confirmed by incorporation in one set of regulations, are perpetuated endlessly and are most difficult to rescind.

The standards for hospital care, for full term and premature infants as prepared by the Committee on Fetus and Newborn, could well be adopted without change by states as the requirements for safe operation of hospital nurseries. The standards, do, however, contain several items on which one might reasonably expect more evidence of correlation between the requirement or recommendation and safe care of babies. These items include: nurse-patient ratio, the use of ultraviolet light, floor-area per bassinet, the use of masks, the need for cubicles in nurseries, the public health value of routine physical and laboratory examinations on personnel. State health departments with their extensive laboratories, experts in sanitary engineering and vital statistics, and their pediatric medical and nursing consultants are in an excellent position to assist in the evaluation of these procedures which have such important clinical and economic ramifications.

Having defined the bases for licensure, the state health departments carry out their responsibilities as an education program. There are, to be sure, some circumstances which require firm handling, but for the most part, hospital administrators and nursing supervisors are quick to see the value of improved facilities and technics. One of the most important factors in the operation of a hospital licensure program is the kind of field personnel employed. The goal of improving hospital care cannot be reached through the use of inspectors who merely check the presence or absence of items on a list. Experience has shown the value of employing highly-trained medical, nursing, hospital administrative, sanitary engineering and dietary personnel, who work as consultants and who are competent to discuss the requirements and to interpret the program.

Hospital administrators, who in the early years of the hospital licensure program in Illinois were reluctant to discuss their affairs with representatives of the State Health Department, have in recent years asked the help of the Department not only in the fields where there is legal jurisdiction, but in others as well. The staff physicians, both obstetricians and pediatricians, have requested consultations on special problems, and have issued standing invitations to the consultants to attend the staff conferences. The apparent success of the Illinois program lies, no doubt, in the fact that the

* U. S. Children's Bureau.

State Health Department has considered as its function the giving of more than bald criticism; it has offered institutes; it has arranged for and paid for post graduate training of key nursing personnel; it has never hestitated to refer borderline issues to committee or to institutions of higher learning.

A third important health department function that has a bearing on neonatal care is the collection, tabulation and suitable presentation of vital data. The employment of statistical procedures is essential in the presentation of the facts on morbidity and mortality and in the testing of the validity of selected relationships. The ability to make reliable statistical studies, however, depends, on the amount and accuracy of the raw data.

By virtue of the long-standing requirements of reporting births and deaths and the social significance attendant upon registration of these events, birth and death information for individual states, counties and the country as a whole is fairly accurate.

The same, however, cannot be said of morbidity data. Due to incomplete reporting and to other factors, there is a lack of information on the health of the people in all age groups who remain alive. Of the reportable disease of public health significance, four are of particular concern in the health of the newborn; conjunctivitis in infants, epidemic diarrhea of the newborn, impetigo and syphilis. And of the four, the most important is diarrhea of the newborn because of the high case fatality rate and the lack of specific therapeutic or even preventive measures. This seems to be a disease of babies in institutions, getting group care—but are we sure? Whenever an epidemic occurs, someone invariably mentions that it is not an institutional problem but a community problem because there is diarrhea in the adult population of the area. What is the evidence? What are the facts? What are the correlations? What is the epidemiology?

State health departments, practicing physicians, hospitals, and the general public as well have a real concern in the solution of this ever threatening problem because, in addition to its clinical hazards, epidemic diarrhea of the newborn is the prime reason for a considerable percent of the costly standards of facilities, personnel and technics, set forth in nursery regulations. The nature of the public health statistical data, available from the Illinois experience with epidemic diarrhea of the newborn demonstrates how valueless the present data is. Despite real effort on the part of the State Health Department, the data which have been accumulated on epidemic diarrhea of the newborn in Illinois hospitals during the past 6½ years are grossly incomplete and contain the glaring inconsistency of a larger number of deaths than cases in 1944 and 1945. Scientifically, these data are worthless, which is rather disappointing when one considers that there were more than 90% births in hospitals, the hospitals were better than average, and the health department was making a concerted effort. No refinements on this material can be made because there is no more data, and it is highly improbable that similar data to even this degree of inaccuracy might be compiled for many other states.

If there were more complete reporting of cases, the experts in statistics could better assemble the isolated bits of information on state and nationwide basis, and perhaps the epidemiologists make some deductions.

Prompt reporting of the disease has an immediate benefit in that state and local health departments can marshal their forces to aid threatened communities. Medical, nursing, sanitary engineering consultants, epidemiologists, and laboratory personnel including virologists, all of whom may be experienced from other epidemics, usually can be made available to assist in handling an outbreak, and in gleaning pertinent research data. Public health nurses can make home visits to infants who might have been discharged from the hospital during the incubation period of the disease. The Illinois Department has given this full battery of service in all known outbreaks, and has arranged for collaboration in virology with the University of Michigan.

Last year, in addition to the amount of direct service rendered, the Illinois State Health Department arranged and financed an institute on epidemic diarrhea of the newborn for hospital, medical, and local health personnel. Dr. Louis Sauer, with abundant experience and real feeling on the issue, and Dr. James Watt, expert on diarrheal disease with the U.S.P.H.S., gave papers. There were other presentations on diagnosis and treatment. There was a panel discussion and the audience took part. The proceedings were printed and distributed. Though the conference did not make any contributions to what is known about the disease, it did succeed in bringing the unspeakable subject to light and dispelled to a marked degree the need for secretiveness about it. The hospital and medical

personnel got a fresh view of the importance of the licensure requirements and the regulations for control of communicable disease. The local health officers, too, had an educational experience, as did we on the central staff. Selected parts of the institute program appeared in the Illinois State Medical Journal, in state and national hospital publications, and the subject was discussed by the Illinois Maternal Welfare Committee and the Illinois Obstetric and Gynecological Society. Subsequent epidemics have been fewer and milder, reporting of cases more prompt, and deaths diminished. This experience, certainly, might have been due to factors other than the institute, but there is no doubt that the institute diminished fear of the health department in increased understanding of the nature of the disease.

Another example from the Illinois experience illustrates other functions of a state health department in improved neonatal pediatrics. This is the Illinois Program for Care of Infants, the evolution of which is a long and pleasant story of cooperation. The State Health Department, knowing the statistics, being familiar with local resources and problems, and having grant-in-aid funds at its disposal, was able to stimulate a large scale program for care of premature infants. The first step was to define the problem statistically and clinically from published data. The second step was to write a workable program. In drafting the program the Department drew heavily on experience elsewhere and received guidance from the Children's Bureau consultant who were familiar with existing premature nurseries and centers throughout the country. The skeleton program was approved by the Council of the State Medical Society and later was expanded in clinical and administrative detail in conference with the local pediatricians, hospital authorities, local health and ambulance company personnel.

The two demonstration centers, with a capacity of about 30 prematures each, have been in operation for four years. Two additional stations will probably be opened this year and salient preliminary arrangements are accomplished in the other regions of the state. The attainment of centers in these latter areas is dependent upon hospital construction programs currently in progress.

Without the State Health Department with its broad interests and powers, this program probably would not have come into operation. The essential functions of the Department in the program have been merely those of a catalyst and coordinator, and, for the needy, the paymaster. The critical details and all of the clinical phases are in the hands of the pediatricians, the family general practitioners, who refer cases from the outlying areas, and the other local health service personnel. The program in the established centers practically runs itself. The paper work has been kept to an almost unbelievable minimum and what little is required is accurately and willingly submitted because it later comes back to the hospital staff in meaningful summaries of operating experience.

The department in this program retains two vital functions: the tabulation of data and the control of funds. The grant-in-aid moneys will soon not suffice to carry the cost of the ever-expanding program and the rapidly increasing per diem cost of hospital care. The function of the Department is then to approach the State legislature, with the data on needs, the statistics on experience, and the facts about costs. When that day comes, I believe that the elected representatives of the people will not be unaware of the fact that prematures in their jurisdiction have benefited from the program and that physicians in their areas value the service.

There are endless examples of state and local health department functions in an all-out attempt to reduce the risks in the first month of life. There is only time to mention antepartum care and prenatal pediatrics, classes for expectant parents, nutrition service, home nursing instructions, public health nursing services, Rh typing, postgraduate education of nurses and physicians caring for mothers and children, milk control, formula room sanitary engineering and the public health aspects of housing. I shall only mention in passing the challenge to further study and the need for mass data on the premature, on congenital malformations as correlated with infectious disease, and on methemoglobinemia and its association with well water.

In state and local health departments there are abundant latent functions which have a bearing on child health. The extent to which these potentialities are activated depends on the wishes of the people, especially the pediatricians.

Chairman Clifford: Our next speaker, Dr. Frederick F. Tisdall, the Director of Research Laboratories of the Department of Pediatrics, Toronto University, has recently visited many hospitals in the United States, Canada, and abroad, searching for ideas on how to improve facilities for the hospital care of infants, his contributions will be of practical assistance to us all.

A Program to Develop and Improve Facilities for the Care of Newborn Infants

Frederick F. Tisdall, M.D. (From the Hospital for Sick Children, Toronto, Ont., Canada.): At the present time we are planning and building a new 550 bed hospital for children in Toronto, which accounts for my particular interest in the physical layout of facilities for the care of newborn infants. During the past two years it has been my privilege to discuss our problems with a number of pediatricians not only in the United States and Canada but in Great Britain and Europe. So many different ideas have been expressed that we are now of the opinion that no matter what we do, in ten years' time we will probably want to change it. The most we can do now is to lay down some well accepted principles in regard to the actual physical layout, and then fit the details in as best we can.

I am going to confine my remarks largely to the problem of the prevention of cross-infection and then, if time permits, deal with some of the other less controversial aspects of the problem. By cross-infection we mean any infection that is contracted in the hospital. There are two main avenues of cross-infection with the newborn—if we disregard the possibility of droplet cross-infection, that is, a baby coughing or sneezing with such vigor that he actually sprays infected droplets for a distance of three or four feet, or, similarly, a nurse sprays these droplets. No nurse with a cold of course should be allowed in the newborn nursery. The two avenues of cross-infection are air-borne—that is, the bacteria being carried through the air for many yards on microscopic particles of moisture or dust; and contact cross-infection, in which the infecting organisms are carried by the nurse, the interne, the attending physician, the mother, or visitors. This means that the infecting organisms can be carried by the hands, clothing, feeding bottles, the thermometer, or any other article which comes in contact with the newborn infant.

What is the relative importance of these two methods of cross-infection? It would appear that certain types of infection, such as gastro-intestinal, are usually spread by contact. Other types, including many virus infections, such as measles and chickenpox, as well as the common cold, are apparently readily spread by air-borne cross-infection. In going about the country we have found it the opinion of all authorities with whom we have talked that from the practical standpoint contact cross-infection is by far the more important. It should be emphasized that the opinions, expressed in nearly every instance were really "impressions" as there have been practically no scientifically controlled observations. However it was the opinion that at least 50% of the cross-infections encountered in children's hospitals were due to contact cross-infections, while many observers placed the figure even as high as 85%.

How are you going to prevent hand-borne cross-infection? I think we can say that there is no question that hand-borne cross-infection can be prevented if a number of relatively simple procedures are carried out. First, you make available running water, soap and scrub brushes. No person should contact a newborn baby without first thoroughly scrubbing the hands. Next, a gown should be available for the person attending each infant so that there is no possibility of carrying infected organisms from one infant to another through the medium of clothing. Of course, adequate care has to be taken in regard to feeding utensils, thermometers, etc., to see that they are sterile. In our new hospital in Toronto it is planned that every infant under 2 years of age will be in a separate cubicle, with an individual washbasin, and the necessary gowns to be put on by the attending persons.

Next, how are you going to prevent air-borne cross-infection? This is a much more difficult and much more controversial aspect of the problem. It is obvious that the number of infants and the number of attendants in a definite area will be a factor in contaminating the air. Therefore a certain number of square feet should be allowed for each baby. I believe that your Committee is recommending that a minimum of 24 sq. ft. be allowed for each infant in the newborn nursery. This would mean roughly a space 6 ft. by 4 ft. Please understand that this figure has nothing magic about it. I believe one could equally justify a figure of 28 sq. ft. or 32 sq. ft. However, the principle behind it is to allow each infant an adequate amount of space around it, and it is felt that the minimum space should be such that each infant would have 24 sq. ft. You will defeat your purpose to a degree, however, if you put your infants all in a row and have the rest of the room vacant.

In regard to air-conditioning this is a great problem with us. I did not know until talking with our architects that the average nursery, or average hospital room, has 1 to 1½ air changes an hour simply through the air coming through the windows or through the doors. I think you

will all agree that in any hospital the air should not be recirculated, that is, all air should be brought in from outside. With air-conditioning, it is customary to have as many as 12 air changes an hour. So that with us, where the temperature gets down at times to 15° below zero, you can see that this creates a financial problem in heating the building which is almost prohibitive.

Studies are going on at the present time in regard to the sterilization of air by the use of glycol vapor and ultraviolet irradiation. At this stage of our knowledge, I think you will agree that while this work is extremely interesting, we are not ready to set down any hard and fast regulations regarding the use of either method. I may say that we are investigating both procedures, having in view their possible use in our new building in Toronto.

One other point of practical importance in the prevention of air-borne cross-infection is the use of a special oil preparation in the laundry. Studies have shown that the number of bacteria in a hospital ward increase tremendously when the sheets or clothing are being changed. There has recently been developed an oil preparation which can be used in very small quantities in the laundry. This keeps down air-contamination due to changing of the sheets and clothing. Similarly, in sweeping floors, oily products should always be used to prevent dust's going through the room.

With all the mechanical equipment, we must remember that success still depends on the type of nursing care. No matter how many washbasins you put in, unless they are conscientiously used by the nurses and also by any other attendant or visitor, you will not accomplish your purpose; namely, the prevention of cross-infection.

In regard to the size of the nursery, I am sure you will all agree that it is better to have a number of small nurseries than one large one. If anything goes wrong in the large room, you tie up your whole institution. Now, what size are you going to have? An attempt has been made to lay down the principle that the nursery should be of such size that one nurse and one helper can look after it. But here immediately you run into difficulties, because obviously if you decide that one nurse and her helper can look after 12 babies, and the 12 newborn infants are all breast fed, the work involved will be definitely less than if the 12 infants are all artificially fed. However, you have to set some figure, and with full realization of the difficulties involved, it has been suggested that the nursery should not exceed 12 cots in size. Do not forget that if in your hospital one nurse and her helper has to look after more than 12 babies, you will completely defeat your purpose if you build your nurseries with a 12 bed capacity. Under these circumstances one nurse will have to do her work in two nurseries and in that case you might better have one nursery twice the size.

We all agree that the nursery should have an anteroom in which no one goes but the nurse. You are all familiar with this practice. The formula room should be entirely separated from the diet kitchen and should be in a part of the hospital which is not close to infection. If it is in a large hospital, it should be looked after by people who have no contact with infectious diseases in the hospital. In addition, you must have a suspect nursery where you put the baby while you are watching to see if it is developing some infectious disease.

The last point for discussion is the premature nursery. It is quite expensive to construct a special nursery with facilities to provide relatively high temperatures and high humidities. However, incubators are now available which are perfectly safe. Some of these incubators bring air in from the outside, heat it, and humidify it to the desired degrees and keep it under a slightly positive pressure in the incubator so that there is little possibility of inside air getting into the incubator and thus being a source of air-borne cross-infection. These incubators can be installed in any ordinary small room, in which of course there should be washbasins and the other facilities already mentioned for the prevention of contact cross-infection.

The Care of the Full Term Infant

C. Anderson Aldrich, M.D. (From the Section on Pediatrics, Mayo Clinic, Rochester, Minn.): Because of the many topics covered in the manual of the Committee on Fetus and Newborn of the Academy, time does not permit me to present and discuss all of those concerned with care of the full-term infants, my assignment in this panel. Moreover, my remarks in almost every instance would have been commendatory since only one or two points are covered in the printed report with which I would take issue. I am, therefore, taking the liberty of saying, "Amen," to the report, as far as it goes, and will proceed to suggest some items which I think should be added

or enlarged on because I believe, to use the chairman's words, "that to build a sound foundation for the future child, family relationship" is decidedly in the realm of modern pediatrics.

Perhaps a new section should be added to the manual with some such title as, "Where the mother fits in with hospital care of the newborn." Whether the baby is to be breast or bottle fed, the mother should take an active part in his nutrition from the start. She will be the major participant soon; and, therefore, she should begin at the beginning. In order to do this she should, if physically able, do most of the actual feeding and ought to be informed about what is going on in the nursery as well. In addition, it is the pediatrician's duty to explain to her at the outset the fundamentals of the physical and emotional status of the newborn and to give her the essential information about early growth and development. In this way only can she be adequately prepared to take over the care of her baby in the hospital and after dismissal from the hospital. Such treatment is medical prophylaxis at its best.

The Mother's Role in the Feeding Program

As soon as his vigor is established, every full-term, normal infant should be taken to his mother. This will usually be possible 8 to 24 hours after birth. The nurse entrusted to this job should also tell the mother something about her baby about as follows:

1. He is a strong, healthy child and hers to feed.

2. He is usually a sleepy human being, not a snapping turtle. Therefore, he should not be expected to take the breast too eagerly at the outset. In fact, it should be explained that many babies are drowsy for three to five days after delivery; that many of them seem wise enough to "sleep it off" while mother's milk is still unavailable and to be casual about sucking until lactation makes it seem worth while to work for their food.

3. Under these conditions, the sensible thing to do is to cuddle the baby comfortably with his cheek against her breast so that if he does begin to root about for food the nipple will be available. This maternal cuddling has a positive value to both mother and baby from an emotional standpoint.

4. During the prelacteal period the baby should be allowed to nurse at each feeding only one or two minutes at each breast. In this way, the nipple will not be irritated by futile efforts before the milk comes in. This precaution decreases the incidence of cracked nipples and their complications.

5. Whenever the mother prepares for a breast feeding, it is important to get herself into a comfortable position in which it is easy to remain for the entire nursing period. This technic needs to be taught to the vast majority of mothers with their first babies and may vary with different preferences of the women as well as with their state of convalescence.

6. If he seems to want it, she may allow the baby to take sterile water or sugar solution from the bottle, as much as he seems eager for. It should be explained that, especially in these early days, he should not be poked, prodded, spanked or snapped in order to get him to take either the breast or the bottle.

The nurse should take it for granted that the mother wants to nurse her baby at the breast. If she refuses to do so, the nurse should express mild surprise but should not argue the matter. The postpartum period is entirely too late for such efforts. If the mother is in doubt, let her discuss the matter with her doctor.

After this introduction by the nurse, during the next day or two, several other matters should be taken up by the medical or nursing staff: 1. If the baby is to be bottle fed, the mother should at least cuddle him in her arms while he is taking his food in order to give him some physical semblance of the breast feeding. 2. The mother should be told that the amount of milk the baby takes will increase steadily during the first week and that except in unusual instances he should not be urged beyond his desire. As a rule, every ounce coaxed down his throat after he definitely pushes the nipple away will be bounced back promptly. However, it is permissible to allow a short resting period after he has finished and then to offer the nipple again to see whether he was full or just tired. 3. The "burping" technic should be explained to the mother if she does not know about bubbles. But also it should be made clear that all babies don't burp! 4. The routine hospital instruction about care of the breasts and nipples should be given.

It is obvious that this introduction of the baby to the mother should, ideally, be done by a nurse with considerable experience, or at least after definite education as to the technics. The use of this method will prevent the common complaints of women that their "baby was just dumped on the bed" and they "didn't know what to do with it."

Each day the physician in charge should make rounds to the mothers to report on the child's progress and to adjust feeding details. He should take the time to explain to her some of the facts about lactation so that she knows what to expect from day to day and the reasons for the routine treatment that the hospital provides.

It is helpful if she is told that marked engorgement does not usually mean copious lactation; at least not until her rocklike breasts have begun to soften. Incidentally, it might be added that successful breast feeding is difficult in such situations and requires great patience and skill on the part of nurses, physicians and mothers. These difficult conditions during lactation need much more attention and investigation than we, in this country, have given them in the past.

Most pediatricians who are interested in breast feeding advise against the use of complemental feedings until the supply of breast milk has proved inadequate. It requires at least five to six days to make this diagnosis under ordinary conditions. Water, or 5% solution of dextrose, is usually given as desired, however. When this is done, dehydration fever or alarming loss of weight rarely occur. (In our experience they occur in less than 0.1% of babies.)

When it becomes necessary to complement the mother's supply or to give complete artificial feedings, it is advisable to have these feedings given with the baby in the mother's arms, not by a nurse. Having the mother herself do the feeding not only saves nursing time but also teaches the mother how to handle her baby before he is turned loose on her at home.

For many years my colleagues and I have made no restrictions as to the amount the baby is allowed to take from the bottle or breast. A newly born baby has an extremely sharp end point for satiety. After nursing for a variable time, he will stop suddenly. This is either for a rest, in which event he will resume nursing after a few moments, or because his appetite is satisfied, in which case urging is useless. For healthy babies strict reliance on the satiety mechanism to determine the amount of food is by far the most scientific method of feeding available at present. This does not mean that the physician's hands are entirely tied from a nutritional standpoint, however, because he can always, on proper indications, strengthen or weaken the prescription for food.

As the time for dismissal from the hospital draws near, mothers should be told that the feeding program at home is usually much easier to carry out than it is in the hospital. Because it has been necessary to bring the baby in to her for feedings at more or less regular intervals according to hospital routines, she has found that sometimes the baby comes in ravenously hungry and at other times he has been so sound asleep that it was almost impossible to rouse him to eat. At home she will be able to feed him when he seems to be hungry. Her first duty will be to find out his rhythm of feeding, whether he is a two, three or four hour baby. As soon as this is approximately evident, she may begin to adjust her daily routines to this natural rhythm of the baby. She will be forced neither to listen too long to his cries when he is hungry nor to awaken him out of a sound slumber to feed him when he is not in the physiologic state for feeding.

In relation to adequate breast feeding, all mothers should be given instruction as to the fundamentals of a diet with its extra supply of protein, vitamins and water. It is also advisable to instruct even nursing mothers as to the preparation of a formula for occasional use as "a gadding bottle." Those whose babies receive complemental or supplemental feeding, of course, should be given explicit instructions as to the preparation of food.

Sometime during the hospital stay mothers should be instructed in how to bathe the child, preferably by demonstration. In hospitals where no baths are given to babies a doll can be used for such demonstration.

Education of Parents

After these efforts have been made to teach the mother about feeding her baby, it is highly desirable that the parents be told something about the physical, mental and emotional status of a newly born baby and what may be expected in his early development. These are matters which each pediatrician will want to handle his own way, no doubt. However, it is an assignment which has not been well handled, I believe, in most cases.

My colleagues and I have developed a plan of giving out brief bulletins explaining the bare essentials during the neonatal period in the hospital. Its advantage is that the instruction is not left entirely to the convenience of the attending physician or resident and the information is always given to the mother promptly. The results are much better, of course, if the doctor takes the time to elaborate on the "bare bones" presented in the bulletins.

In our practice we have emphasized the following points: 1. A newly born baby is automatic and cannot think as yet, but he feels a lot and what he feels influences his emotional reaction to the world. 2. An explanation is made of the state of the special senses and how they grow through development and experience. 3. The cry is a protective mechanism designed to make everyone aware of a baby's needs. Parents and doctors would be helpless without it. It is not spoiling that makes a young baby cry. 4. Babies have an interesting set of reflexes, breathing, sleeping, eating, eliminating and Moro reflexes, which help them to live. 5. Out of the use of these inborn reflexes healthful habits develop later on. 6. Growth is a dynamic process which goes on from within the baby. Its sequence is absolutely fixed, but its rate and amount vary with the individual. 7. Voluntary control of the body proceeds in a cephalocaudal direction which is predictable.

Education of Hospital Personnel

It is obvious that if mothers and fathers are to be instructed in such matters all of the hospital personnel who come in contact with them must first know the subjects thoroughly. I suspect that in this field residents, nurses and even some obstetricians and pediatricians could sometimes stand considerable "brushing up."

Rooming-in Arrangements

This discussion would not be complete without a word about the rooming-in plan. Having a baby and his mother in the same room close to one another or even in the same bed in the hospital is not exactly a new idea. It has been practiced for many ages, and still is, in many hospitals in the world. Some of the obvious advantages of the plan will appear to any pediatrician. A mother's care of her baby will be more personal and intelligent if it starts at the beginning. It saves the nurses' time. It tends to promote breast feeding. Mothers with such experience in the hospital know their babies better on dismissal. The father has a chance to enter the charmed family circle at an earlier time. And finally most of the danger of communicable disease in large hospital nurseries may be avoided. In fact, if rooming-in were widely practiced much of the material in the manual could be eliminated or would have to be revised.

Research

Before closing the subject I think the Committee on Fetus and Newborn will not have done its job conscientiously until it earnestly emphasizes the tremendous need for research in many aspects of the field. It is, in many ways, the most neglected segment of medical interest. Research into the etiology and therapy of neonatal mortality is indicated as much today as was the work on infantile diarrhea in the early years of the century.

A Program for the Care of Premature Infants

Myron E. Wegman, M.D. (From the Department of Pediatrics, Louisiana State University, School of Medicine, and the Charity Hospital of Louisiana, New Orleans.): Specific handicaps of the premature infant and general principles of care are well recognized and only recently have been ably summarized by Gordon and Levine. Reiteration of these principles can serve, however, as a basis for consideration of how they may be applied in the care of all premature infants.

(1) Constant and competent nursing care.
(2) Preservation of normal temperature.
(3) Prevention of infection.
(4) Maintenance of adequate nutrition.

Obviously all of these principles apply, although not so urgently, perhaps, to the care of the normal newborn infant. Where, then, do the differences lie and what special consideration should be given to them in the general program?

Definition of Prematurity

By biologic definition a premature infant is one who has not completed 280 days of gestation and by implication, therefore, is not completely ready for extra-uterine existence. Since the period of gestation is rarely precisely determinable, several clinical criteria have come into use to help distinguish the premature infant. A reasonably effective criterion, which is simple to use, is the birth

weight, and the level of 2500 gm. has been traditionally accepted as the dividing line. Several considerations must be noted, however, since clear cut distinctions have been observed by Dunham with regard to sex, race and plurality as they affect weight at birth. Generally, at a given stage of maturity, females will weigh less than males, plural births less than single births, and Negro infants less than white. While the differences with regard to sex and plurality are probably intrinsic, the differences related to race may be environmental and connected with such factors as inadequate maternal nutrition. In the latter case, a baby at 2500 gm., while not necessarily premature, may still need extra care despite presumably more advanced development. It is probably best, therefore, and least confusing to hospital staffs, to stick to a single criterion for routine admission to the premature nursery. In the Massachusetts State Plan for premature infants, the critical weight is 2268 gm., while in a proposed New York City plan, infants below 2500 gm. would have to be admitted to designated premature units.

The rules now in effect as Charity Hospital in New Orleans are cited as an attempt to provide for all contingencies:

1. All infants who weigh less than 2268 gm. at birth will be admitted to the Premature Station automatically.
2. Upon the birth in the hospital of an infant weighing between 2268 gm. and 2500 gm. at birth, the resident on call will be notified immediately and will decide whether the infant will be admitted to the Premature Station.
3. Any infant weighing more than 2500 gm. at birth may be admitted to the Premature Station, if the pediatric resident in charge believes the infant actually to be premature.

Nursing Care

Constant and competent nursing care means loving attention in the truest sense of the word. It has been pointed out that two hours of nursing care are required every 24 hours for each full term infant, but four hours are the minimum necessary for premature infants. The matter of degree of prematurity is directly applicable here, since the 1000 gm. infant certainly needs far more total special care than the 2000 gm. infant. It is important to have clearly in mind why there is need for the greater time. It is not alone that the premature infant usually requires more time to feed, or that parenteral treatments may be necessary, or that he needs to be watched for cyanosis. All of these things do take extra time, to be sure, but more than anything else it is important for the nurse in the premature nursery not to "cut corners." She must feel secure enough in the time available for her job to carry out each phase of it meticulously, and not to skimp in technic or hurry a feeding. No amount of time available, of course, can replace intelligence and interest, and neither organized plans nor legal requirements can insure good care when these attributes are lacking. There has been extensive experience with legislating minimum requirements for maternity homes and newborn nurseries through official sanitary codes, state-wide standards and the like. Such requirements play an important part in the overall program but they cannot do the whole job. There may be incubators and suction apparatus; there may be an adequate schedule for nurses; there may be a fine formula room. None of these will suffice if real interest and drive are lacking, for then it becomes easy to let the incubator run without checking its operation, to make the nurse's schedule a farce by calling nurses out regularly for "emergency" duty elsewhere, to negate the fine equipment in the formula room by understaffing it to the point where speed-up results in taking unsafe chances.

When I worked in isolated rural areas I saw instances in which excellent nursing care was given to premature infants in their own homes, by their own mothers, who had been instructed by public health nurses and who were working with the most primitive equipment. They did not have the refinements but they did give adequate and loving attention. In the impersonal surroundings of the hospital this kind of nursing care is even more essential.

Proper training of all personnel is obviously basic to a successful program. Ideally all those who work with premature infants should have special training, but if such a goal is impossible of immediate achievement one may demand as a reasonable minimum that the nurse in charge have such training and have the authority to train those under her.

The existing shortage of nurses has caused many institutions to use auxiliary personnel such as nurses' aides and ward maids. If they have aptitude and interest, and are trained and supervised carefully, they can do excellent work.

Preservation of Normal Body Temperature

Preservation of body temperature requires some apparatus capable of preventing wide fluctuations in external temperature and of helping the infant conserve body heat. Standards for incubators which will accomplish these ends have been set up by the National Bureau of Standards, working with the Children's Bureau. Safety devices to protect against mechanical failure are essential. Besides helping to keep the infant's temperature stable and the humidity relatively high, incubators can act as individual isolation units.

It is worth repeating that fine incubators cannot take the place of intelligence or interest in nursing care. By the same token a "premature program" based on the purchase of incubators without proper plans for their use is likely to be futile.

Protection from Infection

Protection from infection raises several problems. Some have been alluded to in connection with nursing care and the need for proper use of the incubator. Space and segregation are also basic. Emphasis must be laid on separation of facilities for premature infants from those for full term or sick infants. Justification for this lies not so much in the possibility of droplet infection extending from a sick infant ward to the premature unit, as in the temptation for indiscriminate interchange of personnel, a greater potential danger.

The premature unit, wherever located, must be a true sanctum sanctorum to which admission is very sharply restricted—for doctors as well as anyone else. To my mind actual location is probably less important than the closed door and forbidden entrance. Usually it is possible, except in institutions caring for only one or two premature infants, to insist on completely separate nursing personnel. It is far more difficult to achieve similar separation for house staff, but the objective should be kept in mind in drawing up schedules.

Use of gowns in the premature unit has less importance from the standpoint of physical coverage than as a stimulus to observe scrupulous technic. Washing facilities, in profusion, must be so strategically located that the staff is constantly reminded of their use. In this connection it seems clear that ordinary masks, as commonly used, have more disadvantages than advantages. While they may act as effective filters for a limited period of time, this is offset by the temptation for a worker with a cold to go into the nursery under the mistaken illusion that the mask will protect the babies.

Another mistaken illusion is related to routine nose and throat cultures for personnel before beginning work in the premature unit. There is little to gain from such a procedure and considerable danger of false confidence. Nose and throat cultures cannot detect viruses and at best they can reveal the presence or absence of streptococci or pneumococci at the time of taking the culture. By the next day, when the culture is being read, the state of the nose and throat may be completely different. Reliance is much better placed on indoctrination of personnel that *no one* with any sort of illness may enter the premature unit. This is perhaps the most difficult of all the rules to enforce. Nursing school policy usually requires students to make up time lost for illness after graduation, if necessary, and many girls will not hesitate to conceal minor illnesses if the potential danger to infants is not made clear. Auxiliary personnel, frequently on low salaries, are loath to lose pay for a day off duty. Better personnel practices, plus arrangements to assign help who have minor colds to duty elsewhere in the hospital, will help prompt reporting of illness.

Proper Feeding

Differences of opinion regarding infant feeding are the traditional battleground of pediatrics. At the 1947 meeting of the American Academy of Pediatrics, Powers presented convincing evidence for the effectiveness of partly skimmed milk with 10% added carbohydrate as a routine feeding for premature infants. In many parts of the country his pupils, of whom the author is one, have used such a mixture with great satisfaction. Others, however, are advocates of full fat milks, of non-animal fats, or of breast milk, although Powers has made clear that the latter is, to say the least, not essential. In all likelihood it would appear that in most instances best results are obtained by the use of the method with which one is most familiar. Within limits, the precise type of feeding used is probably less important than the care with which the food is given and the attention paid to watching the infant's development.

Application of Principles

Just as the foregoing established medical principles guide the actual care of the individual premature infant, so established epidemiologic and public health principles must guide the organization of plans to bring such care to *all* premature infants. These principles may be listed as:

(1) Prompt reporting and case finding.
(2) Immediate provision of proper environment and care.
(3) Planned home placement and follow-up.
(4) Trained personnel.
(5) An integrated program.

Case Finding

It is axiomatic in a sound preventive program that provision must be made for prompt discovery of affected individuals. This requires both a system for reporting to a central authority as promptly as possible the prospective or actual birth of a premature infant, and a mechanism to make available immediately a proper environment and adequate medical and nursing care. In a situation where delay in provision of a proper environment is related directly to increased mortality, reporting by telephone or telegraph is essential. How and where to report must be generally known to all hospitals, physicians and midwives. In turn, such reporting will be futile and unproductive unless the mechanism for placement is clearly defined and can go into action immediately. The person making the report must be told promptly where the baby may go and how he is to be transported. If placement is to consist of the use of a loan incubator in home or hospital the incubator must be available 24 hours a day, as must the services of a person trained in the use of the apparatus.

A typical central point might be the county health office. On receipt of a report of a premature birth a public health nurse goes immediately to meet the physician in the home. Using a special carrying case, if available, or proper wrapping with protected hot water bottles, the baby is made ready for the trip. The nurse will know the nearest center to be used and will assemble the necessary information that should go with the child. In some areas a special "premature ambulance" is part of the equipment of the premature center and can be sent out as needed.

When this mechanism is properly developed physicians soon learn that prompt reporting is attended by prompt results.

Premature Centers

Commonly, placement will mean hospital care and it is therefore essential that facilities for premature infants be of sufficient number and quality to meet established standards. While these may be varied to a limited extent according to local conditions there should be no compromise with basic needs. Standards adopted by a particular community should include considerable detail as to equipment, staff and general method of operation. It is worth reemphasizing that minimum physical facilities and equipment alone do not constitute a premature center. A check list of equipment may be useful for inspection and guidance but a staff which understands the basic principles of care, outlined above, is the most basic need. Number and location of centers will vary with the size of community served, and it will take careful centralized planning to combine wise use of existing facilities with expansion as necessary. Although centers should be widely distributed, they must draw from large enough areas to justify adequate equipment and staff.

Several state, cities and the Children's Bureau have published acceptable standards but mere publication is not enough. There should be trained persons available to the individual hospital or community for consultation and interpretation of the standards. This is another function to which the Academy can contribute, through the efforts of the Committee on Fetus and Newborn, and through the state subcommittees in the same field.

Follow Up

Once the infant is safely located in a satisfactory premature center, plans for his eventual discharge must be considered without undue delay. Excellent care in the hospital may go for nought if home conditions are not investigated and appraised, and if instruction of parents is not undertaken. Both these phases, as is true of later follow-up after the infant has gone home, call for the active services of the public health nurse. Her report on the home allows hospital staff to decide when the infant may safely be discharged. Her instruction of parents in the home should be care-

fully integrated with what is taught the parent in the hospital before the baby goes home. In some institutions public health nurses carry on both the hospital and home instruction through cooperative planning by hospital and public health nursing agency.

A minor but important detail is an adequate report form. Hospital staff and field staff must agree on what information is practical and essential. Forms must not be overloaded with questions or data of limited usefulness.

Social problems which will inevitably appear as homes are investigated require skilled social work. Once a premature infant has attained satisfactory size the sooner he leaves the hospital the better off he is. Prompt attack on an inadequate home situation may lead to real improvement or provision of either a temporary or permanent substitute. Services of competent social workers may be available to some extent through official agencies but local voluntary agencies must share the load.

Trained Personnel

A primary principle of public health practice as well as of clinical medicine is needed for trained personnel. This applies to both medical and nursing staff but at the moment the greater need is probably for nurses. The point has been made earlier that head nurses in premature nurseries must have special training in the care of such infants, but very few places where this type of training may be obtained are in existence. It is only logical that some of the centers designed to give superior care should be set up also for training. Actual demonstration of proper care, combined with student participation, is the most potent kind of education. The Children's Bureau has worked diligently for the expansion of training facilities and additional centers will shortly be opened. A premature center truly capable of giving instruction of high quality cannot, however, "full panoplied spring from the brow of Jove." From our own experiences I can testify that a great deal of preparation is required and that a proper level of performance and instruction will not be immediately forthcoming.

While the creation of training centers to which students can come for long or short courses is a focal point in the program, a good deal may be said for decentralized, local instruction. The pediatric consultant, preferably on the staff of both medical school and state department of health, and a nursing consultant with similar affiliations, can accomplish a great deal by visiting hospitals, reviewing status in the light of standards and actually observing methods of care. Field visits such as these will help to bring the essential activities of the public health nurse, to the attention of physicians. By the same token training programs must be provided for both hospital and public health nurses.

Training and standards are inevitably linked, and general publicity to the medical and nursing professions concerning these standards is an important prerequisite to both centralized and decentralized training programs.

Community Plan

It should be clear that the principles of hospital care, centers for training and demonstration of standards, plans for case-finding and transportation, follow-up programs and public education, all need to be correlated through a community-wide plan. Where such plans have been used they have been richly rewarding, as demonstrated in Massachusetts and Illinois. Other communities have followed these plans with essential local variations. Such plans involve private physicians, hospitals and local community health and social agencies. State and local units of the Academy will profit themselves and the community by energetic and cooperative participation. Obviously, central planning is essential and each participant must not only be aware of his role but also be prepared to accept it.

Logically and properly a community plan should be coordinated by the health department; it has legal responsibility for the health of all the people and should have both organization and equipment to carry out the various procedures outside the hospital itself. The character of health department leadership will inevitably vary from state to state, city to city, small community to small community. Pediatricians must be prepared to offer cooperation or provide stimulus as needed. In the city of New Orleans, as one example, there is smoothly functioning health department-hospital-physician cooperation, despite personnel shortages and a heavy case load.

Details of state plans will necessarily vary; financial support will come in varying proportions from federal and local sources. It has been pointed out that a premature center requires specific equipment and adequate personnel. Provision of these is often beyond the resources of an individual hospital, a local community or even a state. Federal assistance is unquestionably necessary in many

instances. Financial aid will help tight budgets although local government could well contribute more to the attack on a problem with as high a mortality rate as prematurity. More than financial aid is necessary, however. Enunciation, nationally, of generally accepted standards of care, which can be made official by a state or community, will be of inestimable help to local workers who need a yardstick to convince hospital administrators and local government officials of essential goals. Furthermore, many states and local communities will need the aid of specialized consultants who have had experience in program planning. In this way the experience of one state can be brought to the assistance of another.

The role medical schools may play in this program has been alluded to previously. While the very nature of the problem, with its size and need for state-wide coverage, throws the major burden of planning and coordination on the state health department, pediatric departments of medical schools can contribute very substantially. Their function in establishment of training centers is obvious. Not so clear, perhaps, but of great potential value, is the role to be played in consultation, in reviewing standards and in getting out from the four walls of the school into the community, both to spread instruction and evaluate progress.

Summary

Well established principles for the care of premature infants include constant and competent nursing care, maintenance of satisfactory environment, prevention of infection and provision of proper nutrition.

Implementation of these principles is based on specific standards for care, which cover physical facilities, equipment, qualifications and duties of personnel.

There is need for community-wide integrated programs which will insure care that meets these standards, for every premature infant. Programs should include establishment of specialized centers to provide care meeting all standards, and facilities to train personnel both in and outside these centers; decentralized training and guidence in areas other than the centers; complete case-finding and provision for transportation; adequate follow-up; services of public health nurses and social workers. Cooperation, central planning and acceptance of responsibility by health departments, medical schools, private physicians and community agencies are all essential to success.

Conclusions

Chairman Clifford: On behalf of the Academy's National and State Committees on Fetus and Newborn, I would like to extend our thanks to the preceding speakers who have so effectively presented the various parts of a program to improve newborn care. It is evident that many groups have a vital interest in this problem, each has a definite contribution to make but each requires the understanding and cooperation of the other.

We have heard from Drs. Bain and Herbolsheimer of the efforts of the federal and state health groups to improve newborn care. We have discovered that we can receive much valuable help from these sources in solving our individual nursery problems. It is clear that these governmental groups are not sufficient unto themselves but they require our enlightened cooperation in any successful program to reduce neonatal morbidity or mortality.

Much of the material we have heard presented by Drs. Tisdall, Aldrich and Wegman on developing and improving facilities for the care of full-term and premature infants will be incorporated in the forthcoming manual on newborn care the Academy intends to produce. The second draft of this manual is in the process of being revised but the process takes time. We hope to have it ready by the Academy meeting in November.

In the meantime the State Committees on Fetus and Newborn are organized and anxious to start work. To satisfy this need your Academy Committee submits the following suggestions for the immediate activation of state programs to develop and improve facilities for the hospital care of newborn infants:

I. Through cooperation with state and local health agencies:
   1. Have the infant's birth weight placed on and made a part of the official birth certificate.
   2. Prepare a standard form for the reporting of hospital deaths and survivals.
   3. Raise the percentage of post-mortem examinations of newborn infant deaths.
   4. Investigate full term and premature infant deaths.

5. Suggest that adequate facilities for premature infant care be a requirement for all maternity hospitals.
6. Approve and list centers for premature care and/or assist hospitals to establish or enlarge and equip a premature center.
7. Investigate the problem of payment for the care, transportation, pediatric services and after-care of premature infants.
8. Educate the public concerning good infant care.
9. Attack the problem of the training of nursing and medical personnel and the training of nurses aides, nurse maids and auxiliary workers.
10. Investigate the possible use of M.C.H. funds for studies and investigations related to the problems of the full term and premature infant.
11. Try to increase the number of breast fed infants through prenatal education.
12. Participate in hospital planning for the state.
13. Support and interpret nursery requirements for participation in funds under the Hospital Construction Act.
14. Give support for adequate hospital licensing laws administered by the state health agency. Support a program of consultation service to hospitals by the state agency to accompany licensing. Offer assistance in the development of recommended standards for hospitals by the state agency. Participate in developing the code for licensing.
15. Offer to serve on state health department advisory committees concerned with nursery and newborn care.
16. Offer to serve as consultants or staff members in premature care programs.
17. Assist in training programs for doctors, nurses and social workers in premature programs.

II. Encourage medical and nursing schools and state postgraduate programs to place more emphasis on the care of the newborn infant; full term and premature.

III. Organize an immediate attack on the problem of epidemic diarrhea of the newborn along the lines suggested by Regulation 35 of Chapter II of the New York State Sanitary Code (approved by the New York State Public Health Council, January 16, 1948). This regulation received the approval of the individual members of the Committee on Fetus and Newborn of the Academy prior to its passage.

New York State Sanitary Code

Chapter II

Regulation 35. Precautions to be observed for the control of diarrhea of the newborn. It shall be the duty of administrators of general hospitals or child caring institutions, proprietors of maternity hospitals or maternity homes, and physicians and nurses responsible for the care of normal newborn and premature infants in general hospitals or child caring institutions, or maternity hospitals or maternity homes, to take all reasonable precautions to prevent the introduction and spread of diarrhea of the newborn, including the following:

a. Formulae and other fluids offered to newborn infants in hospitals or child caring institutions, or in maternity hospitals or maternity homes shall be poured into individual feeding bottles at the time of preparation, and a nipple shall be attached to each bottle and covered with a cap. The entire product shall then be subjected to terminal heating by steam under pressure of not less than 15 pounds (121° Centigrade or 250° F.) for not less than 5 minutes, or at a pressure of not less than 6 pounds (110° Centigrade or 230° F.) for not less than 10 minutes, or by flowing steam at a temperature of not less than 100° Centigrade (212° F.) for not less than 30 minutes. The temperature of the formula or fluid, as determined by periodic examination, shall not be less than 93° Centigrade (200° F.) at the end of the heating process. The nipple cap shall remain on the bottle until the time of feeding. If fruit juices, or formulae containing lactic acid, meats, or cereals are given to newborn infants, they may be offered without such terminal heating, but shall be prepared with and stored in pre-sterilized equipment.

b. Normal newborn and premature infants born in a hospital or maternity hospital or maternity home shall not be kept in the same nursery, room or ward with sick infants or older children. Nurses giving care to infected patients shall not come in contact with infants in the normal

newborn or premature infant nurseries. No infant born outside the hospital or maternity hospital or maternity home shall be admitted to the nursery for well infants, except after isolation for a period of one week. An infant born to a mother who has diarrheal or respiratory illness shall not be admitted to the nurseries for normal newborn or premature infants.

c. An infant suspected of having diarrhea of the newborn shall be promptly removed from the normal newborn or premature infant nurseries, and kept under isolation precautions. If, after observation, diarrhea of the newborn is found to exist, such infant shall then be transferred to an isolation nursery.

d. Individual equipment shall be provided for each infant except for the weighing scales, which shall be freshly covered for each infant. Common bathing and dressing tables are prohibited. The use of racks, carriers, or bassinet stands for holding or transporting more than one infant at a time is prohibited. Physicians and nurses shall wash their hands under running water before and after coming in contact with any infant.

e. Nursing care shall be given to each infant at the bedside. Space shall be adequate to give such care, provided that the total nursery floor space shall average not less than 24 square feet per infant, or the infants shall be placed in individual cubicles.

f. No room used as a nursery shall house more than 12 infants, nor shall such a room intercommunicate with other rooms used as nurseries. There shall be running hot and cold water for handwashing in each room used as a nursery, with the flow of water controlled by elbow, knee or foot valves. No nurse shall give care to more than 12 infants and their equipment.

Enacted January 16, 1948, to be effective January 1, 1949, except that the enforcement of either or both subdivisions "e" and "f" may be deferred for an individual institution for a period not later than January 1, 1951, by the State Commissioner of Health upon request of such institution.

Discussion

Question from the floor: Explain the need for and the mode of operation of a suspect nursery as opposed to an isolation nursery.

Dr. Wegman: The chief idea about a suspect nursery is to make it easy for the physicians, the mother and the nurses before the physicians get around to do something for the baby and before we are sure the baby is sick. Once we are sure, then the baby ought to be put into a true isolation nursery. It is a double safeguard because it isolates the really sick babies from the baby more dangerous from the standpoint of exposure.

Question: Explain the block system in the newborn nursery where there are a large number of babies in one room.

Dr. John McK. Mitchell: This is a system which has been established by head nurses in some nursery wards where there are a large number of babies in one room. In some nurseries, for example, you may have 48 to 60 babies. The head nurses have divided these babies into blocks of eight, assigning a single nurse to care for the babies in that particular block. All the nursing equipment and things which will be used for that block are kept separate from those in the rest of the nursery. By this system it is possible for the head nurse to trace down a particular nurse who in the care of any baby may be found to have an infection that may have been the source of a cross infection. It has been found in several big nurseries that by the use of this method they have been able to cut down the number of cross infections quite materially.

Chairman Clifford: You all appreciate the tremendous amount of detail that goes into the preparation of any set of standards. It would be very boring to go through them line by line. It is something that will have to be threshed out in small groups, many times working far into the night, until a satisfactory compromise can be worked out. I think what you carry away from a meeting like this is the important methods for combatting infection which is the greatest enemy of our nursery population. The importance of contact infections and the introduction of infection into our nurseries cannot be overlooked. We find very little difference of opinion among workers as to the need of various methods by which this should be controlled. First and foremost in the minds of all is adequate soap and water. We can do more with this many times than with laboratory equipment. In talking with many men in various parts of the country I find that in certain states unfortunately there has been a rather dictatorial attitude on the part of a rather hysterical health department because of the recent criticisms as to the outbreaks of pediatric diarrhea in those communities,

with the result that new standards are being instituted which, if enforced, would put most of our hospitals out of business. We feel there has been too much criticism.

Many pediatricians are not convinced that six babies is the ideal number of babies in the premature nursery. Many are not convinced that 30 square feet is the proper diameter for a premature nursery. Many feel that with that type of equipment you could take as many babies as you have room for. This question means that licensing authorities can create almost impossible standards for small hospitals. What can be done to prevent large and small hospitals from carrying out extensive building alterations? Personnel is an important thing. This is a point I got from talking with men throughout the country. Talking this over with Dr. Bain, her point of view is that public health authorities do not intend that this should be held as a weapon over the small hospitals which could not be defended on any scientific basis.

Dr. Bain: The health departments are not concerned with putting out of business the small hospitals that are struggling. What they are concerned with is to offer consultation service and to maintain such standards as will be good for hospitals. There is no desire to act as a policeman. The idea is to offer them some help so they can give good service.

Round Table Discussion

ASTHMA IN CHILDREN

FRANCIS SCOTT SMYTH, M.D., *Chairman, San Francisco, Calif.*

Chairman Smyth: It is our purpose at this Round Table Discussion to discuss asthma in children with special emphasis on the practical aspects of such care.

A literal interpretation of the word asthma is "to breathe hard." This is the symptom in labored respiration after violent exercise, with oxygen lack in high altitudes, so also the lack of oxygen caused by circulatory and cardiac disturbances. Such usage of the term, "labored breathing" also implies a primary obstructive phenomena in the lungs, or a pneumonia. Thus, we find our differential definition requires further limitation. Asthma is really a symptom with many possible causes. So, for our own purposes of definition, we are going to limit the subject of asthma to those patients whose labored breathing is due to edema, secretions, and smooth muscle spasm induced by allergic sensitivity.

No element in the diagnosis is more important than the history of the patient. A good history cannot be obtained in one interview but is the result of persistence by the physician and of cooperation and understanding by the parents. A diary-like history kept by the mother will be invaluable. Many times we have interviewed anxious parents when the child was having an acute asthmatic attack, and got nowhere on the family history. You suspect there may be a bilateral allergy inheritance but you can elicit no information as to a constitutional inherited factor. This is equally true of the initiation of symptoms. The parents may deny any other allergic symptomatology, but as they begin to understand the problem, you will obtain further information extremely valuable for your study. The physician wants to know the season of the year in connection with the onset of symptoms, the locus of the first attack, has the child had repeated colds, any dermatitis of an allergic nature, etc. Once the intelligent mother has understood the problem, her observations can be as accurate as those of the physician, and in several instances, I have seen her come up with a solution of certain phases of the problem which has been very apt.

It seems unnecessary to mention the importance of the physical examination. In a sense, it is the clinician's scientific approach, i.e., accurate observation which not only clarifies the differential diagnosis to a great extent, but also brings to light the nutritional status, contributing infections, and the general make-up of the child. These are often of the utmost significance in any program designed to bring relief from the asthma, as well as to assure robust health.

The third method of study involves laboratory tests and this includes dermal or skin tests. If obstruction of the bronchi and bronchioles is the cause of asthmatic dyspnea, a low hemoglobin, and/or an anemia will aggravate the oxygen lack, so the blood count is important. The white blood cell count and differential are traditionally significant. The peculiar rise in eosinophils associated with foreign protein reaction, is well known as is the general increase in white cells with infection. However, it should be borne in mind that the total count and eosinophil percentage are subject to wide variation in younger children. Often the eosinophils are higher after the acute phase of the attack than during its height, when they may leave the blood stream to become fixed in the shock organ—the lung.

Hansel has demonstrated a valuable laboratory test which few of us should neglect, that is, the use of the stained nasal secretion for eosinophils. The assumption that colds are always of an infectious nature is challenged by Hansel's nasal secretion test. It is surprising to find what a percentage of these nasal smears indicate an allergic component or possibly a purely allergic origin.

Skin tests are a most interesting and valuable aid, but as in the case of most of our laboratory tests, they must be interpreted in relation to the patient. For the most part they are associated with the allergic constitution, but they may be found strongly positive in individuals with few or no allergic complaints, or they may be weak in a patient with marked symptomatology. Furthermore, the patient may react to allergens to which he is unlikely to be exposed. We must look to some

From the Annual Meeting of the American Academy of Pediatrics, Dallas, Tex., December 8-11, 1947.

common denominator chemically to account for certain group skin reactions and Drs. Black and Deamer will have more to say on this subject. So, like other ancillary tests, skin tests are valuable if studied with relation to the patient, and they do not obviate sleuth work regarding offenders. We know too, that they may vary, depending on the state of the child; and we know that benadril, or other drugs, can block them. No roentgenologist would want to give a complete interpretation of a film without knowing something about the patient. This is equally true of skin tests; they must be interpreted in relation to the patient.

Certainly the offending allergens related to asthma may be found in a wide range of materials. Cooke is prone to classify asthma as extrinsic, or intrinsic, and by that classification refers to factors (allergens) from without the body or, as in the case of ineffective agents (viral or bacterial) to intrinsic asthma. One can then refer to infective or non-infective, although clinically, in children we often have a mixed picture. However, it must be admitted that with the exception of tuberculin allergy, our knowledge concerning the antigen reactions in infections is not so readily understood as with the non-infective, extrinsic allergic type.

The allergens of extrinsic asthma may be inhaled or ingested, occasionally injected. Therefore, our skin tests will include both inhalants and foods. We know now that positive skin tests are rarely found under four months of age, that epinephrin-like or anti-histamin drugs may reduce the skin reaction. We know also that the reaction varies in intensity on different skin sites. All of which does not lead to the position that skin tests are of no value, but rather that they may be of considerable significance, if properly interpreted with the entire study of the particular patient.

A valuable diagnostic aid in asthma is the roentgenogram, but it should be accompanied by a fluoroscopic study of diaphragmatic action. The frequency with which infection complicates asthma and the so-called allergic pneumonia, which is apparently related to the plugging of bronchioles, makes the use of X-ray valuable for certain patients.

To sum up, there are many factors involved in dealing with asthma in children: physical infections, emotional and environmental, to name the most important ones. While it would be very nice to put these factors in a neat compartment and tell ourselves these are all we have to worry about, we still have the blood count, nutritional status, the role of infection, and many children in themselves can be complicating factors of equal importance with any allergic study.

Dr. Bowen, Houstin, Tex.: Dr. Hansel has a special eosin-methylene blue stain, a very quick method, but we have found it can be simplified as follows:

Solution: 1-200 eosin—0.30 gm. eosin in 60 cc. methyl alcohol; 1-1000 Methylene blue—0.06 gm. in 60 cc. methyl alcohol; 95% ethyl alcohol; distilled water. For convenience all solutions should be in dropper bottles.

Technic: Smear out secretion so as to be not too thick on slide. Allow to dry in air or gently over flame. Stain for one minute with 1-200 eosin solution. Then add sufficient distilled water to take up staining solution and cover slide completely. Allow to stand one minute. Then drain off and flood with water until all free stain is removed. Flood with 95% ethyl alcohol and drain off. Then immediately stain with 1-1000 Methylene blue for one minute and repeat with distilled water as above and let stand for two minutes. Then remove excess stain with distilled water and flood again with 95% alcohol. Dry and examine under oil immersion. Eosinophils will stain with easily recognized red granules.

Dr. Poncher, Chicago: The use of drugs in the treatment of the acute asthmatic attack. Briefly, we are dealing with two basic objectives: I. The relief of bronchial spasm; II. the relief of bronchial occlusion caused by edema, tenacious mucus, and mucus plugs.

I. The Relief of Bronchial Spasm

A. Bronchodilators

1. Epinephrine (1:1000). I don't believe we need to discuss the efficacy of this drug in relieving bronchial spasm. It is generally admitted to be one of the most valuable at our disposal. A word of caution should be sounded concerning dosage however.

While the dosage of all autonomic drugs has not been scientifically determined in children, there is little justification for the large doses commonly employed. Smaller doses repeated at more frequent intervals are much more effective than a single large dose. Children between the ages of two and five years will be benefited by dosages of 0.1 to 0.2 cc. and from five to ten years from 0.3 to 0.5

cc. It is rarely necessary to exceed these doses and if the attack persists the dosage may be repeated in 15 to 30 minutes. In some so-called "epinephrine-fast" cases which fail to respond to a single dose, bronchial spasm is sometimes effectively relieved by using small doses of epinephrine every 15 minutes for three or four doses.

2. Intramuscular Epinephrine in Oil (1:500) may give a more prolonged action but relief is not immediate and its action is too irregular for the acute attack. It has been used in doses of 0.3 to 0.5 cc. to prolong the bronchial dilation achieved with subcutaneously administered aqueous solution (1:1000) and it is effective from six to eight hours. Local reactions have limited the popularity of this type of therapy, particularly where peanut oil is used as a base.

3. Intravenous use of epinephrine has been advised for the severe attack but this is a potentially dangerous mode of administration. Its use in children may be questioned.

4. Aerosol epinephrine (1:100) has been effectively used by creating a mist of fine, divided particles by means of a special all-glass nebulizer. The persistence of the aerosol mist may be enhanced by administering the medication in a 5% solution of glycerine. Unpleasant side effects such as dryness of the pharyngeal mucosa, tachycardia, tremors, nausea and gastric distress may result from the mode of administration. While this is an effective method of providing relief from bronchial spasm, it is apt to be used injudiciously because of the ease of administration and frequent side effects occur as a result. The parents should be forewarned concerning frequency of administration if this method is utilized.

5. Ethyl-Nor-Epinephrine (Butanefrine), first investigated by Tainter in 1934, may be substituted for epinephrine to avoid many of the vasopressor actions and other side effects. Clinical reports on its use substantiate the claims for its bronchodilating action and its effectiveness in the bronchial spasm of asthma. It may be used subcutaneously, intramuscularly, or by means of aerosol. Accurate dosage has not been established for children but 0.25 to 0.5 cc. of a 1:500 solution may be injected subcutaneously or intramuscularly and it may be employed as an aerosol in doses of 0.5 cc. of a 2% solution.

6. Other sympathomimetic drugs like neosynephrine (0.25%), propadrine (1.5%), and privine (0.05%) have been effectively used as aerosols in 0.5 cc. doses but adequate data concerning their comparative effectiveness with epinephrine are not available.

7. Aminophyllin is an effective bronchodilator and has great value in the treatment of the acute asthmatic attack. For immediate relief it may be given intravenously in a dose of 0.006 gm./kg. body weight in 10% to 25% dextrose solution. The dose should be given in volume of 10 to 20 cc. and injected very slowly to avoid side reactions. Care must be taken to avoid getting the solution outside the vein. Aminophyllin is available commercially in ampoules in two strengths 0.25 gm. and 0.5 gm. in 10 cc. and 20 cc. saline. Doses larger than 0.25 gm. are seldom indicated at any age period in childhood. Priegal has reported on the use of aerosolized aminophyllin with some success. Ten to 20 cc. of a solution containing 0.25 to 0.5 gm. of aminophyllin was nebulized continuously. The side reactions noted with intravenous administration of the drug were not observed. The smaller dose (0.25 gm.) is advised in children. Aminophyllin may be given rectally or orally if immediate effect is not the therapeutic goal or if sustained relief of bronchospasm is desired. A dose of 0.25 gm. in older children is adequate as a suppository or a suppository of this dosage can be split lengthwise for infants. The dosage interval is four to six hours. Franklin effectively combined aminophyllin (0.25 gm.), sodium phenobarbital (0.05 gm.) and benzocaine (0.03 gm.) in a suppository for children with asthma. Orally, aminophyllin may be administered alone in doses of 0.05 to 0.1 gm. or effectively combined in the following prescription for older children:

Rx	Aminophyllin	100 mg.
	Phenobarbital	16 mg.
	Ephedrine Sulfate	16 mg.

and administered in four to six hours intervals.

8. Ephedrine sulfate in doses of 0.015 to 0.03 gm. combined with phenobarbital or other sedatives to minimize nervousness may be used to sustain the bronchodilating effects by other methods of treatment. Tolerance of this drug varies considerably in children and care must be taken to avoid insomnia and nervousness with its use. Fatigue, emotional instability and loss of sleep predispose to further attacks of asthma.

9. Atropine sulfate is generally contraindicated in asthma as it causes a thick, tenacious sputum

with continued use. Occasionally in an acute attack it may be used in conjunction with epinephrine and other sympathomimetic drugs to relax bronchospasm with striking results. It should never be used repeatedly due to the drying effect it has on mucous membranes. The dosage of atropine is 0.02 mg./kg. orally and 0.007 mg./kg. by hypodermic route.

10. Antihistamine Preparations. Benadryl, pyribenzamine and other antihistamine drugs have been used in acute attacks of asthma without striking success. Their use is not without possible deleterious effects because of their atropine like action in the drying effect they have on mucous membranes. These drugs as a class have a questionable place in the treatment of an acute attack of asthma and the effects that have been observed are difficult to dissociate from their sedative action. Hydryllin is a combination of benadryl and aminophyllin and any beneficial effect observed is more likely due to the aminophyllin than the antihistamine action. No reliable data are available to indicate that histamine has any value in the treatment of bronchial spasm due to asthma.

11. Oxygen and Helium Oxygen Inhalation. In severe intractable asthma (status asthmaticus) or recurring bronchial spasm, in spite of symptomatic treatment oxygen in 50% to 70% concentration may be indicated, especially in the presence of pulmonary emphysema brought about by persistent bronchial constriction. Oxygen should be humidified as the drying effect on the bronchial mucosa has been demonstrated when administration is directly from the tank. Barach has clearly set forth the clinical and physiologic indications for the inhalation of oxygen enriched atmospheres in persistent and recurring attacks of asthma in his excellent treatise on "The Principles and Practices of Inhalational Therapy." The same author has also provided the indications for helium (80%) oxygen (20%) mixtures in intractable asthma. Since the velocity of movement of gas through a restricted orifice (bronchial spasm) is inversely proportional to the square root of the molecular weight of the gas, oxygen diffuses faster in an atmosphere of helium than nitrogen (helium is 1/7 the specific gravity of nitrogen). The dramatic clinical relief which follows the use of oxygen helium mixtures in intractable asthma is based on the reduction of the negative intrapleural pressure produced by forcible breathing against a constricted orifice. Reduction in the negative intrapleural pressure is important since it increases pulmonary and mucosal edema and secretion of mucus in the bronchi. The effect of breathing a mixture of helium and oxygen in intractable asthma is often dramatic and striking.

II. *Relief of Bronchial Occlusion by Edema, Tenacious Mucus and Mucus Plugs*

In the preceding discussion the pathologic physiology of breathing against a constricted orifice with its attendant increase in negative intrapleural pressure and cupping action on the bronchial mucosa and pulmonary tissue was cited. Such changes are not the sole causes of endobronchial obstruction and wheezing in the acute asthmatic attack. Bronchial secretion may be excessive in the presence of an acute allergic attack where the respiratory tissue serves as the shock organ directly due to inhaled allergens. Inflammation of the bronchial mucosa may also result from dust or nonspecific irritants or from an infectious bronchitis.

Whereas the first part of our discussion was primarily concerned with the relief of bronchial spasm and its sequelae, this phase of our therapeutic approach is directed at the problem of relieving endobronchial obstruction due to tenacious and inspissated mucus.

One of the most effective means of treating milder forms of endobronchial obstruction is to facilitate movement of secretions from the tracheobronchial tree by the cough reflex. The most important agent for this purpose is water (ingested and inhaled). A physician often gives serious attention to the use of expectorants while neglecting to maintain an adequate hydration of the patient by proper fluid intake. In fact, the use of medicaments inducing vomiting which is advocated as a therapeutic measure by some may defeat its purpose, since it enhances the development of dehydration and thereby increases the viscosity of the mucus. Inhalation of water vapor as steam or cool moisture from a humidifier is indicated.

Where humidifiers are not available they may be improvised by using a Vaponephrin Atomizer and inverting a liter of water so that it drips into the atmozer by gravity. No clamp is necessary to regulate the flow as a 27 gauge needle inserted through a cork stopper on top of the atomizer will serve this function. The nebulizing force may be supplied by a bicycle pump, air compressor, or an oxygen tank.

Fluid nebulized as an aerosol is more apt to reach the deeper portions of the bronchi as it is not so likely to condense. Medications such as epinephrine or aminophyllin can be added to this vapor

as desired. Priegal has suggested use of ammonium chloride as an aerosol in an effort to liquefy the tenacious mucus and to facilitate its expectoration. He recommends 10 cc. of a 5% solution for this purpose. We have had no experience with this, but it is conceivable that in the future increasing use will be made of aerosols as a convenient and effective way of administering medication to children with asthma. Caution must be observed lest one substitute one form of irritation for another. Therefore, critical and careful clinical trial is necessary prior to the endorsement of any new procedure or medication.

Four drugs deserve special recognition as orally administered expectorants in asthma. If possible they should not be prescribed with opiates or the belladonna alkaloids and other drugs which depress the cough reflex or increase the viscosity of the sputum. They are ammonium chloride, sodium or potassium citrate, ipecac and potassium iodide. All are efficient expectorants and decrease the viscosity of the sputum. Whenever cough mixtures are employed in the treatment of the asthmatic attack they should be designed to exalt rather than to depress the cough reflex. The fact that mixtures containing opiates and belladonna alkaloids in full therapeutic doses have been employed without more serious complication testifies to the integrity of the defensive force of the respiratory tract rather than to the efficacy of the therapy. Where opiates or sedatives are employed they should be prescribed alone as indicated, with restraint, and for specific conditions. It would appear entirely rational, for example, to employ sedative drugs so that the patient does not exhaust himself and thus cough less efficiently. The employment of sedations under these conditions may be associated with respiratory depression and therefore close observation for signs and symptoms of hypoxia is indicated.

In severe cases, bronchoscopic removal of thick, tenacious, mucus plugs may be indicated when other measures fail or at once if the condition of the patient warrants such a procedure (atelectasis).

The presence of an acute exacerbation of asthma in the presence of an acute upper respiratory infection (particularly those due to streptococci or pneumococci) may call for therapeutic attack upon the infection. Aerosols of sulfonamide drugs have been used in such cases without striking effects and they have the further danger of precipitating a reaction in a vital organ if sensitivity to them exists. The administration of aerosolized penicillin has been more extensive. Its bacteriostatic action is not only local but adequate therapeutic blood levels are obtained by absorption from the pulmonary tissues. Fifty to 100,000 units of penicillin may be dissolved in 1 cc. of physiological saline and given as aerosol every three to four hours. Siegal, Priegal, Vermilye, Barach, Bryson and others, have reported on the use of penicillin aerosols in acute upper respiratory infections in asthmatic patients and their reports indicate that the therapy is worthy of further critical trial with carefully selected cases. Recently inhalation of penicillin dust by means of a special oronasal mask has been reported by Krasno and Rhodes (Science **106**:249, 1947). This method obviates the need of a nebulizing force, since the negative pressure developed by normal inspiration distributes the crystalline sodium penicillin (50-100 mesh) throughout the bronchial tree. The inhalation of fine dust aerosol particles has the advantage of protracted topical effectiveness and gives a greater concentration of penicillin per unit area of infected mucosa. Such therapy is an adjuvant and not a substitute for measures designed to produce bronchial relaxation and liquefaction of mucus. The question as to whether the administration of penicillin by aerosol predisposes to future sensitization has not been settled.

The use of sedation has a definite place in the treatment of the acute asthmatic attack and must be judiciously employed and carefully watched. In a good many instances the attack is intensified by the apprehension and fear that many children experience with an acute attack. Barbiturates are commonly employed for this purpose and it is always advisable to use sedatives of this type with epinephrine or ephedrine. Demerol is a particularly useful sedative in the acute asthmatic attack because of its antispasmodic action in addition to its sedative effect. It may be given in doses of 15 mg./kg. hypodermically. The dosage by mouth may range from 10 to 70 mg. depending upon age and weight. The use of morphine should be condemned in the acute attack of asthma in children.

Finally, it should be emphasized that the habitual use of medication without an attack on the central etiologic factors in asthma is poorly conceived management. These factors are to be discussed in detail by other members of the round table. Drugs should occupy a useful but limited place in the therapy of asthma; they do not serve as substitutes for careful diagnostic study to which every patient with asthma is entitled. Finally, it is not possible for me to conclude a discus-

sion on drug therapy without warning that overmedication is always a hazard and not infrequently contributes to inept management of the asthmatic child.

J. Harvey Black, M.D., Houston, Texas. The same pollens that cause hay fever also cause asthma so that, if one knows the pollen situation so far as hay fever is concerned, he may use this knowledge interchangeably in the study of asthma. Since the pollens are in the air seasonally there is a definite seasonal variation in pollen asthma. They are definitely seasonal in their onset and duration.

There are, however, in my experience, a great many children who have a seasonal asthma, due to a certain pollen, who also have a perennial asthma due to something else and the parent comes in with the story that the child has asthma throughout the year. You may find, on questioning, that these children have a definite exaggeration of their symptoms at a certain time of the year corresponding to a definite pollen season. This is a point of diagnostic importance which may be elicited if carefully searched for. A great many children, as a great many adults, are sensitive to more than one thing. The problem of etiology is simpler in children than it is in adults, possibly because they have not had their asthma so long and have not become sensitive to so many things. But it is not uncommon to find them with a mixture of seasonal and perennial asthma.

Seasonal asthma, due to pollen, is more frequent than we used to think. A great many of the earlier workers in this field talked about asthma in children as being due largely to foods and not to inhalants and a good many of us started out with the idea that we could pay attention largely to foods. But we become more and more convinced that there are many inhalant factors involved in the production of asthma in children and that pollens, as etiologic factors, are found much more frequently than we originally thought. Why they should not be found as frequently as pollen hay fever I do not know but pollen asthma in both children and adults is less frequently seen than is pollen hay fever.

Most of us believe that asthma fundamentally is the same as hay fever. That it differs only in its location and the tissues involved. Fundamentally the mechanism is the same. If the mechanism is the same, the etiologic factor the same, inhalation of pollen the same—and certainly a considerable amount of pollen which is inhaled must get down into the bronchial tree—my difficulty is in understanding why we have so little asthma from pollen and so much hay fever from it. What the answer may be, I do not know.

This brings up a correlative statement regarding what Dr. Poncher has just said about the antihistaminics. Why they should be so effective in hay fever, for example, and so ineffective in asthma, to me does not make sense. If our theory that histamine is the ultimate cause of the allergic symptoms, if the basic mechanism of asthma is the same as that of hay fever, and if histamine is the cause of symptoms in both, this difference in effectiveness is not explained.

I had an experience some time ago which cast some doubt on our concept of the action of these antihistaminic drugs. A man who had a typical autumnal hay fever due to ragweed pollen, had used pyribenzamine with a great deal of success during the ragweed season. After the ragweed season was over he continued to have a great deal of nasal symptoms from a perennial allergic rhinitis due to house dust. Oddly enough, pyribenzamine gave him no relief from his house dust allergy. Now this was the same patient and the same nose. It was not a question of whether as much of the drug got into the bronchial mucosa as in the nasal mucosa, as has been suggested, to explain these variations. In this instance it was not a matter of distribution nor dosage. The only difference was in the antigen and the antihistaminic worked beautifully in the ragweed hay fever and not at all in that due to house dust. To me, the histamine theory just doesn't quite pan out and there must be other factors or other activities of these drugs involved.

The important pollens in this part of the country are very much the same as those elsewhere with a few notable exceptions. Ragweed accounts for more of the hay fevers and more asthma than any other pollen.

The grasses involved depend upon the part of the country in which you live. Here, bermuda and johnson grass are the chief offenders and, while we have a number of other grasses, they are practically of little importance. I am one of those who believe that timothy pollen may be used in the treatment of all the grass patients. There is a great deal of evidence to the effect that timothy contains a composite antigen which includes the antigenic fractions of bermuda and johnson grass. We have used it in this way for a number of years and find it satisfactory in spite of the fact that timothy is not found in this part of the country.

The ragweeds which cause most of the trouble in this part of the world are the giant and dwarf varieties. Here again I think there is so much relationship that it makes no difference whether you treat patients with one or the other or a mixture of the two. Western and southern ragweed are found in the South and can be protected against by the giant or dwarf pollen.

I am not at all sure that I have ever seen asthma due to careless weed. The pollen is here but appears to be a comparatively minor factor even in the production of hay fever.

Tree pollen can cause asthma but we see comparatively few of them. In this part of the world we have a very important problem in a cedar that blooms in January and February or, in South Texas, as early as mid-December. Here it is an important midwinter hay fever problem with some asthma due to it. It is not of great importance elsewhere. There is no other pollen in the air at that time and the diagnosis is made easily. I have seen only one or two patients with asthma from cedar; hay fever due to cedar is common.

A problem which arises with the ragweed sensitive patient who has asthma instead of hay fever is that the asthma usually comes two to three weeks after the onset of the ragweed season. If it is associated with hay fever it begins later than the hay fever, stops sooner, is more readily controlled and usually is nocturnal and mild. The patient who has a ragweed asthma without hay fever also starts much later than the hay fever patient—often after the peak of the pollen season is past. I know of no adequate explanation for this late onset of symptoms.

We have here a fall blooming elm which pollinates in September and complicates the ragweed season. It is such a frequent cause of trouble that we use it routinely in testing patients with a history of autumnal hay fever or asthma. It is of little importance elsewhere.

The recognition of the pollen factor can be based largely on the periodicity of the attacks or the periodicity of exaggeration of symptoms. Skin tests are very dependable; you will rarely find a patient sensitive to ragweed who gives a negative skin test. It can happen. Conversely, there are occasional patients who give positive skin reactions to ragweed pollen who are not sensitive clinically. But skin tests with pollen in asthma, as in hay fever, are quite dependable.

Now just a word about molds. For several years there has been conducted a survey to find something about the distribution and seasonal prevalence of molds and which ones were abundant and of importance. My own conviction is that molds are important factors in the production of hay fever and asthma in some parts of the country. In other parts of the country they seem to have less significance. Here in Dallas, for example, I have tried for several years to find some one whom I could prove clinically sensitive to molds. I'm still looking for one. We find a great many patients who will react by skin test to mold extracts and we have treated some of these extensively with mold extracts. So far, I have never been able to prove that we have helped one of them. While I am skeptical about the importance of molds in this area I am quite willing to believe that they may be very important in other parts of the world. It may be that with increased knowledge about them and with better extracts with which to work, we may have to revise our idea.

William C. Deamer, M.D., San Francisco, Calif.: The previous speaker has indicated that he finds inhalant allergy more common than food allergy. That is also our experience. Whether this is because we are not pursuing the possibility of food allergy diligently enough or whether it is a fact, I cannot be sure but I have tried to keep an open mind on the possibility that food allergy occurs more often than we are finding it. At present, we are of the impression that inhalant allergy in children is considerably more common.

Dr. Black has discussed one of the principle varieties of inhalant allergies; namely, pollen allergy. There remains another category of inhalant allergy which perhaps is the most common cause of asthma in children, and that is house dust. Immediately you may think that this isn't one category—that house dust is a mixture of things and it is not correct to think of it or speak of its as a substance. This is perfectly true but it is nevertheless convenient to consider it as one problem, rather than as separate problems of, for example, epidermal or cotton linters allergy.

There is a mixture of substances in house dust but the deficiencies of our knowledge are shown if we try to subdivide house dust into its component parts either by skin test or by analysis. We find it impractical and what the missing links or substances are, I do not know. There seems to be an aging factor in many of the substances, particularly in kapok and cotton linters, which is important.

There may be mold factors which are behind the scenes and Rackeman and others have suspected and commented on that. Rackeman, Cohen and others have pointed out the importance of kapok and

cotton linters in a house dust sensitive patient. I mention it especially because patients we test to kapok and cotton linters by and large do not give positive reactions to these substances even when they are bothered by them clinically, as the majority of house dust sensitive patients are. I think that is a common experience. This is an instance then illustrating the fact that we should not lean too heavily on the skin tests, either positive or negative. There is probably no substance in an ordinary house which is quantitatively as common as kapok and the closely related cotton linters with perhaps the single exception of wool. The mattresses, the bed springs, the studio couches, the day bed, quilts and comforters, are usually composed of kapok or cotton linters entirely or in large part.

How does one recognize a house dust sensitive patient? I think we have almost got the habit of assuming that if the patient has asthma he is house dust sensitive. This is probably something for which we should be criticized but it is an out-growth of the fact that most patients are sensitive to house dust both by scratch test and by clinical trial. It comes out in the story, for instance, that the child was better or worse with a change of environment. This implies at least that a food allergy is probably not foremost in the picture. A child goes away on vacation and we'll say, improves markedly. On coming home there may be an aggravation of his symptoms. Should he go to the hospital with asthma, a large part of the improvement that he makes is probably due to the fact that a hospital is physically a different environmental situation than his bedroom. I find it useful to ask the parents if they noticed any benefit or aggravation if they moved from one home to another. If they have moved recently or frequently, the benefit or aggravation associated with the move will tell the same story—that an environmental factor is concerned and that approaching the problem on the dietary basis isn't likely to be rewarding. This is especially true when moving day, during which time a great deal of house dust is stirred up, is the day the child picks to get his asthma. If that is the case it is pretty good clinical evidence that some environmental factor, probably house dust or one of its component parts, is concerned. The house dust patient very often wakes up in the morning and sneezes during that period between waking and breakfast, when he is dressing and first getting about in the morning, and why that should occur, I have no idea. The concentration of house dust in the air at that time is no different from any other time or certainly no different from what it has been during the night when the patient has been relatively free from symptoms.

All patients, however, are not relatively free during the night. Some have paroxysms of sneezing in bed at night, which are worth investigating. They are not brought out unless you ask about them and of course many of them have a night cough, which, while not associated with any audible wheezing means asthma to me just as much as though it were a clear-cut attack. The cardinal symptoms of asthma are coughing and wheezing and the wheezing need not be so loud that it is audible without a stethoscope. In many instances I am sure you have heard asthmatic sounds by stethoscope in a child who was not wheezing audibly. This is asthma of a different degree but it still is asthma.

In carrying out the house dust environmental control program we like to clear the decks and not try to be too specific about one substance. The frequency of the skin test being negative to kapok and cotton linters is an example of why one should not lean too heavily on skin test. We feel that starting with the bedroom is important and very logical in view of the amount of time a child spends in that one room. For example, if this room in which we are now were to be rendered suitable for a house dust sensitive patient we would start with the rug and rug pad, which happen to extend from wall to wall and both of which are tacked down. This would probably meet with some resistance from the mother because it would be in her mind a difficult job to get rid of the rug and pad and the room would not look well if she did it. To me, it would be of cardinal importance to do it and I would tell her that she could replace the rug with two or three washable cotton, bathroom type mats, which are not unattractive and which serve the purpose of a rug very adequately. We would remove the drapes as contributing unnecessarily to the dust. While these Venetian blinds do not contribute any dust because they are of wood and metal, they are excellent dust catchers and unless the mother wants to go to the trouble of cleaning each individual leaf, which I am sure we would not trust her to do, we would recommend their removal because they are a series of shelves on which house dust rests. We would permit a simple glass curtain or screen which could be cleaned easily and which would serve for privacy. We would get encasings for the bed, mattress and the box springs and they would be of adequately thick material with zippers on them. Such

encasings are obtained from different companies, the two with which we are most familiar are the Allergen-Proof Encasings Company of Cleveland, and the National Allergic Sales Company of New York. There are encasings which are sold in various department stores, some with zippers and some without, but I am not impressed with the durability of the materials with which they are made. For a pillow, we would recommend those made of glass fibre, which have recently become available, are not too expensive and contain no allergens. These would not require an encasing. If the mother prefers, she can get an allergen-proof encasing for the pillow similar to that on the box springs. She can also have the choice of a rubber latex or sponge rubber pillow. If she begs off buying any pillow, claiming the child is not used to a pillow or always puts it on the floor, we would not be impressed. We would still recommend that she have some suitable pillow available because we see all too often the following sort of thing happen. The child catches a cold or breaks his arm or for some other reason has to spend some time in bed. That is the time when he wants to sit up and play and color his books and that is just the time when the mother will bring in not only one but three pillows, sacks of the material to which he is sensitive. This adds asthma to whatever put him in bed in the first place. So we explain that a pillow should be available even though not used. Then we would search the room for stuffed toys, teddy bears, etc., which from their fuzzy outside or their kapok inside, might contribute dust and would cause trouble particularly when one realizes that the child places the toy intimately close to his nose. We would recognize the child's right to some toy and would explain that many such toys may be of rubber or wood or metal. Not so easy though would be the answer to the mother's claim, when we ask her to get rid of the cat or dog, that the child has to have a substitute pet. We have recommended goldfish or turtles as non-allergic pets but that has never met with any great enthusiasm.

It just so happens that animal epidermal substances do not lend themselves well to extraction. Possibly for that reason the scratch test to the epidermal substances is frequently negative. We must not use the negative skin test as an excuse for permitting a cat or a dog to remain in the environment of a child with asthma. They are too famous as causes of trouble. We have a sign in our clinic that reads, "Patients with asthma are not permitted to have cats or dogs or feather pillows." It does not add "if they are skin test positive"—it just says they are not permitted to have them. This, I realize is something difficult to enforce and it is only because it has paid off so many times that I stress it as much as I do. I am sure that it is worth while.

I think then, we have covered what we would do: we would not permit animals, we would look at the toy situation, the floor covering, the bedding and the encasings.

I will now show a slide which shows the amount of time a child spends in his bedroom. It indicates 10½ hours, but I submit to you that many children spend 12 hours out of 24 in their bedrooms. When dressing and undressing, sleeping and playing, are counted it is very close to half of their entire lives in one room. That is the reason the room must be fixed perfectly and that is why it is important to start with the bedroom.

Take the other half of the child's life. You see five hours are spent at school, a place where there isn't any house dust at all. There are no rugs, there is no kapok or cotton linters, there are no cats or dogs, there are no rug-pads made of cow hair, there is no mohair (goat hair) covering the furniture. There may be lots of dirt, sand, earth, wood splinters but there is no house dust and that is a very important distinction to make.

The mother keeps thinking of house dust as dirt the child tracks in on his shoes or that comes in from the outside. It is not that at all and earth strewn all over the room would not cause any trouble, but empty the vacuum cleaner or the carpet sweeper out on the floor and the child will not only sneeze but will probably have asthma if he is house dust sensitive and is an asthmatic.

The other four hours out of that portion of time spent away from home is spent out-of-doors and of course there is no house dust there. In the other rooms of the house where the child spends his remaining three to four and a half hours, there may be house dust but you see what a small proportion of the total exposure to house dust this represents. Some of those rooms, such as the bathroom or kitchen are very poor sources of house dust in comparison to bedrooms. Therefore, house dust control begins in the bedroom although it may have to extend to other rooms such as the living room.

The next slide is one modified from that in Dr. Fineberg's text. I think you will see that it mentions specific causes of asthma and precipitating causes. The specific causes are the usual allergens, particularly the inhalants we have just been discussing. The precipitating causes are many and

include such other things as fog or other climatic factors, exertion, upper respiratory infection, smoke of any type, fatigue and emotion. These, I like to think of as the things which pull the trigger of a gun, thereby causing an explosion (asthma) and the specific causes as the bullets in the gun. It is true by and large that if you remove the bullets these precipitating factors are usually unable, by themselves, to cause asthma. Added to a certain amount of specific causes, however, they are capable of causing trouble. I think this concept explains why we see parents searching for a climate to take care of the child's asthma, since they have observed that climatic factors play a part. They think of climate as a cause; more often it is a trigger phenomenon and a child can be rendered comfortable in a climate the mother thinks is unsuitable.

The next slide is a graphic representation of the story a mother tells in her language. She says her child has one cold after another and some go into bronchitis. The bottom of the slide shows, I think, the actual situation. What she has called a "cold" is usually not a cold but is asthma in an unrecognized form. Occasionally, however, there is an actual upper respiratory infection which is identified as such because it is shared by other members of the family. The mother is correct about once in five times in saying her child has a "cold." The other times it is allergy in one form or another. Even when the child has pneumonia, this is largely asthma with mucous plugs of such a size and number that atelectasis and dyspnea occur which resemble pneumonia. Frankly, I think very often it is hard to tell whether the child does have pneumonia. The justification for this concept is shown when following the removal of the "bullet" frequent "colds" no longer occur. And it is gratifying to find that when the child has a true upper respiratory infection it is not followed by asthma. That is the story we get from many of our clinic and office patients.

Crawford Bost, M.D., San Francisco, Calif.: Is the man in pediatric practice able to take care of an asthmatic child properly? Does he know how and where to start and what to do? I think the answer is yes. The practitioner is the one who most often sees the child in his home, and as Dr. Smyth and Dr. Deamer have mentioned, this is a peculiar and particular advantage. Treatment of the acute attack—so important in the minds of the parents—is so small a part of the problem of the asthmatic child. We must be thinking of a plan for study of the asthmatic child even during the acute attack. Frequent writing of such a program for parents while at the bedside of the child revealed surprisingly little variation for the individual patient. On this basis grew the "Program for Care of the Asthmatic Child," a copy of which you each have today.

A. Prophylaxis heads the list because the items outlined serve to warn, alert and acquaint the family with the nature of asthma: (1) Warning physician and parent alike, that colic, eczema, rhinitis, chronic sneezing, chronic nasal itching, cough on exertion, frequent colds, persistent night cough, etc., may all mean allergy; may all be predisposing the child to occasional asthma. (2) Alerting parents concerning the certain pitfalls and wise avoidances for the allergic child. Here we mention such things as dust exposures in the home, house pets, avoidance of known allergens in the way of foods, etc. Emphasis is made that such avoidances may actually be the means of preventing attacks. (3) Acquainting the parents with the nature of asthma is necessary in order to make such emphasis understandable. Having found that most texts seemed complicated to parents, one of our associates wrote the four page story of allergy which you have been given today. This, I think, is quite readable and helps us to acquaint parents with the knowledge that many things are possible other than treatment after an acute attack. If they care for more detailed information texts are recommended.

B. Next is outlined a "Plan for Study." This lists a mode of attack for the individual patient. It is based on the assumption that the parents are acquainted with the facts already mentioned, plus a careful history by the physicians. In addition to this we solicit the patience of the parents in carefully observing the course of the ailment in their own child. By so doing there is often added information of great value in the prevention of recurrent attacks.

The plan for most children includes—and we think in the order of their importance—the institution of several general procedures:

(a) Dust eradication. This has been covered by Dr. Deamer.

(b) Pet elimination. Dr. Deamer mentions only goldfish and turtles as pets for allergic children. I always add snakes, which helps to impress parents.

(c) Improved emotional patterns. Both the family and the child need to learn to avoid excitement and tension, both during and between attacks. Much can be done to improve such thinking in the home.

(d) Parents as clue finders with proper instruction as to how and what to look for: We have found that parents often furnish the clues that eventually lead to a better approach to their child's asthma. A calm but investigative interest helps parents understand asthma.

(e) Food eliminations. These are tried when they seem indicated and always on the basis of history.

(f) Scratch testing. You will note on the outline that we do all of the previously mentioned things before we do protein testing. We do careful, and repeated, scratch tests. We use a complete set of fresh and carefully prepared potent allergens. We emphasize again repeated testing. Quite often, I think, we can properly interpret the tests. We do not do intradermal tests. This is the point at which we ask the consultation of the allergist.

(g) Role of respiratory infection. Always in the mind of the parents, and often in our minds, is asthma associated with respiratory infection? I do not know the role of infection in allergy. We should ask some of the allergists here to tell us; but, I do know that in childhood there is the child who has asthma only during the respiratory season. At the same time he is having asthma other children in the community are having asthma; five or six of them have it almost no other time.

C. Treatment of the attack. Dr. Poncher has covered this topic today, but I would like to add a word about early treatment. I think we should teach our parents to recognize the early signs of the attack and to institute treatment promptly. I believe this can save a great deal of difficulty and emotional disturbance to the child.

Dr. William W. Belford, San Diego, Calif.: I seem to be the kibitzer on this program. I am very happy to have heard what the previous speakers have said, and approve of it, but there are still gaps in the program. We see all sorts of people, Navy and Army people, people on the move, people working in war plants, all looking for help, looking for a climate where their own or their children's asthma will be better. Many of them have had very fine studies made by the best allergists. Some have had no studies; others from a little treatment to too much. You have all seen patients who have been over-treated.

On the whole, the people who putter around have no routine, no patterns, and no common sense outlook on life. They are somewhat out of control and a bit "screwy," and view their condition from an emotional standpoint. Parents must have a tolerance for troubles and an ability to adjust to them, as, for example, they must if they have a diabetic in the family. Successful treatment depends on the cooperation of the whole family.

Sometimes you are appalled when you get the child's point of view. This patient has had lots of treatment and is thoroughly scared: another doctor, another needle, more trouble, perhaps more restriction, more pushing around, and most of it unpleasant. Dr. Bost says it can be made more bearable, as well as sensible. You can allay the child's fear and instill confidence.

During the war years, particularly from 1942-1944, we had the emotional tensions in the family; the father was out in the Pacific, and the child was going from bad to worse because the mother was so scared of what might be happening out there. She couldn't get up early enough to see what the bad news in the paper was, and for awhile that news was bad. In addition, we had the blackout, lots of planes tearing through the air night and day, and everything else to keep the children and their mothers constantly scared, and it was a bad mess all around.

We had a home in San Diego, formerly a preventorium, which we used for some of these problem children. The minute the emotional tension was removed these children would bloom; their asthma and other difficulties would disappear; they could eat and sleep. I do not feel they are "cured." It will recur in other situations.

The working mother was another factor in our problem, and we had hundreds of them. The child was constantly being hurried: through his meals, going to bed, going to school, do this, do that. Then, there was the father, who thought he was going to avoid the draft and didn't. This turmoil involved the children until it was settled one way or another, and sometimes wasn't settled until the father returned home. The broken home is another difficult situation, where the child is farmed out with some relative or in a boarding home, and there is emotional imbalance.

Another group we saw and still do, is made up of those children who do badly in school because of constant nagging by parent and teacher, who demand perfection. We don't get to first base with these patients, even with the best of allergy treatment, suggestions, and home situations. There is something else to correct.

Parents become angry with the physician for many reasons. The one that hits first is the amount

of money allergy treatment entails. Sometimes they have spent tremendous sums. Have any of you thought what the drugs alone have cost you for these treatments? What should you charge these people for your services, particularly if you haven't obtained results, and you are still in difficulty? Some of them have been to quacks and through all sorts of situations, which sometimes worked, and you wonder why. Dr. Black mentioned some odd situations, where a father had one disorder and his son another, and he couldn't explain it.

As Dr. Black said, parents protest they didn't want to take the treatment and cannot see the point in all this. It takes more starch out of me trying to convince them of what should be done for their children, than carrying out the treatment, arduous as that is. You must catch the parents when they will be somewhat receptive to your urging, as Dr. Bost does.

I would like to have over-exertion and fatigue, which you say to avoid, defined. What do you mean? What is the normal fatigue point for one child, what for another? How are you going to set it? Often when you try to limit the fatigue of these children, it only adds up to emotional tension. A curious anomaly is that these children can play baseball and run with little or no trouble or fatigue in the preventorium or away from home when the activity in the home seems to play hob with them.

Thank you.

Question from the floor: "What is the role of infection in allergy?"

Chairman Smyth: At the beginning of our discussion, mention was made of bacterial allergy. Except for sensitivity to tuberculin, our concept of bacterial allergy is not on very firm scientific ground. Streptococcal sensitivity, as judged by the skin test to the toxin (Dick Test), is being studied. But the possibility of sensitization to bacterial products, as causes for asthma, rhinitis, etc., is not widely accepted. Infections may aggravate or favor allergic phenomena not in a fashion similar to, for example, ragweed pollen; but by their increasing the permeability and vascularity of the mucous membrane. Vaccines, on the other hand, may be non-specific in their action. It would be my conception that just as Besredka could vaccinate successfully by oral administration with typhoid bacilli if bile were given preceding the vaccine, there is a greater absorption of unaltered protein in infants whose intestinal mucosa has been irritated by diarrhea (Schloss). In the respiratory tract, especially in children, asthma is often associated at onset with infection. It may be assumed that the infection acts as a trigger phenomenon by making for a greater absorption from the respiratory mucosa.

Differentiation of "infectious" from allergic colds can thus be confusing. In this connection the study of the nasal smear for eosinophils is important.

Question from the floor: "Is the incidence of severe asthma greater in the age eight to twelve years than in the one to five year group?"

Chairman Smyth: I believe we see severe asthma less complicated by infection in the older children. And in the younger, one to five year-olds, the infection may be of considerable severity. As these children grow older they develop some degree of street immunity and their asthma is less complicated by severe infection.

Question from the floor: Are there more asthmatic children in the age group one to five years than in the eight to twelve group?

Dr. Bost: I would answer, yes. It may be that by eight to twelve years the patients are going elsewhere, but certainly in my office I see many more little than big children with asthma.

Dr. Black: No one has ever established the fact that there is a true infectious allergy. We have infections associated with allergy but no one has shown that the infection is the cause of the allergy. There certainly is true bacterial allergy but no one has shown that asthma results from such a bacterial allergy. We see many patients who have attacks of asthma precipitated by colds. There are many others in whom asthma is ushered in by sneezing and rhinorrhea which is entirely allergic and not a true cold. Even when it is a true cold which precipitates the attack this acts simply as a "trigger" mechanism and is not otherwise related to the attack.

Question from the floor: Discuss persistent vomiting in an attack of asthma resulting in acidosis.

Dr. Deamer: The average child does not have persistent vomiting in the acute attack of asthma. Vomiting associated with asthma alone is most often related to the medication used. However, the

child who vomits apart from asthma as well as with asthma, makes one think of gastrointestinal or food allergy.

Question from the floor: Do you see in some of these food sensitive patients episodes of vomiting like periods where they will go into dehydration?

Dr. Deamer: Yes, but one has to distinguish whether the effort of breathing during the attack has resulted in vomiting and also what role the over-use of drugs plays in vomiting.

Comment: Colds do the same thing. A child is scared—he gets scolded at school—comes home vomiting.

Dr. Belford: I disagree thoroughly. One of the common symptoms is nausea and vomiting. Children can vomit at will, and do, and you cannot do anything about hydrating them. This is where I differ somewhat from Dr. Poncher. A sedative is needed to relieve the child's excitement then you can begin to get your liquids in and control the attack. Many of these children complain of stomach ache, and continue to growl about it, and you all know it is the onset of the asthma attack. If you can get water in with perhaps a little nembutal to quiet them, you will head off much of that vomiting. You can't do much by giving drugs by mouth after they get to vomiting.

Dr. Poncher: I have no objection to sedative drugs—the thing I cautioned about was the over-use of sedation. I am thoroughly in favor of sedation, as I mentioned in my category of treatment.

Dr. Belford: That would be my approach to persistent vomiting. Give them enough sedative to quiet them so they would not be so hard to handle.

Chairman Smyth: Dr. Belford's comment on the use of sedation is to the point because sometimes you see much apprehension and anxiety.

Question from the floor: Do pollens remain alive in winter in homes, schools, etc.?

Dr. Black: Yes, they do.

Question from the floor: Is human dander a significant factor in your experience?

Dr. Deamer: No, no one feels it is. It might be mentioned, going into the history again, that Van Leeuwen originally thought human dander was our universal allergen and that brings up this next question.

Question from the floor: Have any of the speakers had any experience with the use of special vacuum cleaners for removal of inhalant allergins in the home?

Dr. Deamer: There is no doubt that a very good vacuum cleaner is a highly desirable thing in an allergic household. The ones in which the air passes through a water trap are the good ones.

ADDRESS CHANGES OF MEMBERS OF THE AMERICAN ACADEMY OF PEDIATRICS SINCE THE LAST PUBLICATION OF THE FELLOWSHIP LIST

Dr. Harold Abramson
145 E. 61st Street
New York 21, New York

Dr. Carlos Andrade Marin
Garcia Moreno, 1354
Quito, Ecuador

Dr. Juan Basora-Defillo
Box 4341 (B.O. Sta.)
Santurce, Puerto Rico

Dr. Warren F. Belknap
1809 South Main Street
Royal Oak, Michigan

Dr. Charles Bradley
University of Oregon Medical School
Portland 1, Oregon

Dr. Carlos E. Castillo
Apartado No. 39
Maracaibo, Venezuela

Dr. Virginia M. Cobb
208 N. Douty Street
Hanford, California

Dr. Dante Costa (Associate Member)
Rua Carvalho Azevedo 18
Apt. 201
Lagoa, Rio de Janeiro, Brazil

Dr. Reuben A. Craig
Armstrong-Landon Bldg.,
Kokomo, Indiana

Dr. George E. Dash
R.F.D. Boothbay, Maine

Dr. Osanah de Olieveira
Conselheiro Spinola, 9
Salvador, Baía, Brasil

Dr. Robert Devereux
Berwyn, Pa.

Dr. Joseph Garland
8 Fenway
Boston 15, Massachusetts

Dr. David W. Goltman
1428 Madison Avenue
Suite 1
Memphis 4, Tennessee

Dr. Samuel Goldberg
3219 E. Prince Avenue
Tucson, Arizona

Dr. Louis E. Heideman
12244 Dexter Blvd.,
Detroit 6, Michigan

Dr. George V. Herrman
Plaza Time Bldg.,
411 Alameda Road
Kansas City 2, Missouri

Dr. N. William Hing
326 Stockdale Street
Flint 4, Michigan

Dr. Marion G. Josephi
2629 Dwight Way
Berkeley 4, California

Dr. Owen A. Kearns
120 East Palm Street
Monrovia, California

Dr. H. H. Liberman
Westwood Wilshire Professional Bldg.,
1245 Glendon Avenue
West Los Angeles, California

Dr. Raúl Moreira
Felix da Cunha, 1136
Porto Alegre, Rio Grande do Sul, Brazil

Dr. Daniel J. Pachman
8133 S. Jefferey Avenue
Chicago 17, Illinois

Dr. Juan Carlos Recalde Cuestas
Urquiza 1086
Rosario, Sante Fe, Argentina

Dr. Oscar Reiss
715 North Roxbury Drive
Beverly Hills, California

Dr. Julio Schwarzenberg
Pl. Bulnes 1302, Depto. 122
Santiago, Chile

Dr. Walter B. Seelye
Harborview Hospital
9th at Jefferson
Seattle 4, Washington

Dr. Bernard H. Shulman
2320 Foster Avenue
Brooklyn 10, New York

Dr. Irwin P. Sobel
952 Fifth Avenue
New York 21, New York

Dr. Albert F. Stein
7353 Sheridan Road
Chicago 26, Illinois

Dr. J. Mel. Teixeira
Av. Rui Barbosa 716
Instituto Fernandes Figueira
Botafogo, Rio de Janeiro, Brasil

Dr. Dorothy Fraser Wheeler
1666 E. Eighth Street
Chico, California

Dr. Sherl J. Winter
U. S. Naval Hospital
Long Beach 4, California

Dr. Samuel M. Wishik
Johns Hopkins University
Baltimore 5, Maryland

Dr. G. H. Withers
2920 Santa Monica
Albuquerque, New Mexico

Dr. Benjamin J. Wood
Dollar Title Building
Sharon, Pa.

Dr. Henry H. Work, Jr.
5106 Columbia Pike
Arlington, Virginia

Dr. John Zahorsky
R.R. #2
Steelville, Missouri

Pediatrics

VOLUME 2 JULY 1948 NUMBER 1

SPECIAL FEATURE SECTIONS

THE PEDIATRICIAN AND THE PUBLIC

EDWARDS A. PARK, M.D., *Editor*

Dear Dr. Park: It is pretty generally agreed that medical practice in this country has been based on the premise of free choice of physician by the patient, and maintenance of a satisfactory, direct, doctor-patient relationship without the intervention of a third party. At present the opponents of tax-supported, government-controlled medical care are convinced that some form of voluntary, prepaid medical insurance constitutes the best means of protecting our free choice of physician and direct doctor-patient relationship principles.

Some 40 years ago the beginnings of voluntary, prepaid medical care plans were made in this country. These beginnings were made in the Pacific Northwest. They had their origin here because of the peculiar demands of the local, hazardous industries of lumbering, mining and fishing. Contract practice came into being, and received tremendous impetus from the Industrial Insurance Law which was passed in Washington in 1917. Competition for contracts became so intense during the depression period which started in 1929 that vicious methods threatened the structure of medical practice in the State, and it seemed likely that most of the physicians would be relegated to practicing as salaried individuals under a form of health insurance. It was at this time that the various county medical service bureaus in the State of Washington were revived or organized. In Pierce County (Tacoma) a Bureau had been in continuous operation since 1917, and in King County (Seattle) one had been in operation from 1917 to 1925. These bureaus had been organized primarily to contract for work under the State Industrial Insurance Law, and to guarantee a free choice of physician to the workers who belonged to the Bureau. In May 1933 the King County Medical Service Bureau Society was instrumental in organizing the King County Medical Service Bureau to compete with existing contract groups, and to block a proposal by an insurance company for selling insurance and hiring physicians to render necessary medical care.

Since then the movement has grown so that at present 23 medical service bureau plans cover most of the populated area of the State. At the outset the majority of physician contract holders turned their contracts over to the Bureaus in an honest effort to further this plan of providing satisfactory medical care on a free choice of physician basis to workers of low and moderate income. Some few individual and groups, however, for personal and/or pecuniary reason, retained their private contracts, preferring not to cooperate with the major portion of the medical profession in the plan for improving professional and economic medical standards.

The Bureaus are non-profit organizations, providing prepaid medical and/or hospital care in accordance with various type of plans. The participating doctors (about 85% of the licensed physicians of the State) agree to furnish this care to such subscribers as may come to them as private patients, and to accept from the Bureaus as full compensation for such care the fees fixed by the Bureaus, at no further charge to the patient.

The Medical Service Bureau plan for prepaid medical care has been successful. About one-third of the employed of the State are subscribers, a figure made the more remarkable, since 48% of the employed are not eligible for coverage by virtue of the fact that they are employed in groups of four or less. Free choice of physician has been preserved, since such a large proportion of the licensed

physicians are participants. Furthermore, if a patient is not satisfied with his initial choice of physician, he may choose such other(s) as he may wish, and the Bureau will remunerate them, provided they are participating doctors.

I suggest that you read Simpson's monograph, as well as a condensed copy of the current contracts as provided through the King County Medical Service Bureau. These are of great interest. In many points the King County Medical Service Bureau plans are quite like the Health Insurance Plan of New York, which you published some months ago.*

The success of this pioneer program was made possible in large measure by the willingness and unselfishness of most of the holders of private medical-care contracts in turning over those contracts to the Medical service Bureaus at their (the Bureau's) inception, thus preserving for the subscribers the right of free-choice-of-physician and of direct doctor-patient relationship.

I hope that this information will be of some value to you.

Sincerely yours,

(signed) JAMES W. HAVILAND, M.D.

---

* Ann Kent, M.D., M.P.H., and Dean A. Clark, M.D., Maternal and child health benefits under the health insurance plan of greater New York, J. Pediat. 30:756, 1947.

TRENDS

IN HEALTH LEGISLATION AND ADMINISTRATION

By JOHN P. HUBBARD, M.D., *Contributing Editor*

This and subsequent descriptions of events and trends are intended to be unbiased and factual, presenting both sides of controversial matters so that conclusions may be formed from critical appraisal of things as they are. These statements do not necessarily reflect the opinion of the writer nor are they to be interpreted as official opinion of the Academy.

NATIONAL HEALTH ASSEMBLY

DURING the first four days of May, the National Health Assembly met in Washington. The Assembly which was called by Federal Security Administrator Ewing, at the request of President Truman, opened in a charged atmosphere. As expressed by one observer: some of the delegates came to Washington with eyebrows at top mast, freely airing suspicions that the four-day conference was a Democratic political expedient. That the Assembly avoided many of the pitfalls lying in its path was a notable achievement. Evidence of its success appears in an editorial of the Journal of the American Medical Association* which credits Mr. Ewing and his associates for having dispelled the doubts and anxieties which had originally existed.

May 1, not only marked the opening of the Assembly, it was also, by Presidential proclamation, "Child Health Day." The subject of child health was therefore the central theme of the opening luncheon which was presided over by one of the past presidents of the Academy, Dr. Lee Forrest Hill. Dr. Hill reviewed for the Assembly the Academy's nation-wide survey of the existing medical facilities and services available to children. He also described briefly the formation of the continuing committee—the Committee for Improvement of Child Health—charged with the responsibility of analyzing the hard-won facts and translating them into an action program.

The Assembly's assignment was a formidable one: to review the whole field of health and to set forth the feasible goals which might be realized in the next decade. In order to cover as much ground as possible, 14 sections were formed. The subjects assigned to these groups and a list of their Chairmen are an interesting array:

Section 1. What is the Nation's Need for Health and Medical Personnel? Algo D. Henderson, Chairman.

Section 2. What is the Nation's Need for Hospital Facilities, Health Centers and Diagnostic Clinics? Charles F. Wilinsky, Chairman.

Section 3. What is the Nation's Need for Local Health Units? Haven Emerson, Chairman.

Section 4. Chronic Disease and the Aging Process. James R. Miller, Chairman.

Section 5. A National Program for Maternal and Child Health. Leona Baumgartner, Chairman.

Section 6. A National Program for Rural Health. Joseph Fichter, Chairman.

Section 7. What is the Nation's Need for Research in the Service of Health? Andrew C. Ivy, Chairman.

Section 8. What is the Nation's Need for Medical Care? Hugh R. Leavell, Chairman.

Section 9. State and Community Planning for Health. Florence R. Sabin, Chairman.

* J.A.M.A. 137:146, 1948.

Section 10. Physical Medicine and Rehabilitation. Henry H. Kessler, Chairman.

Section 11. What Can Be Done to Improve Dental Health? Ernest G. Sloman, Chairman.

Section 12. A National Program for Mental Health. William C. Menninger, Chairman.

Section 13. What Can Be Done to Improve Nutrition? Frank G. Boudreau, Chairman.

Section 14. A National Program of Environmental Sanitation. Arthur D. Weston, Chairman.

There will be no attempt in this column to review or even to pick out the high points of all of the section discussions. The Journal of the American Medical Association has announced that its pages will carry the reports of each of the panels. There are, however, three section reports which merit special consideration.

The focal point of the whole Assembly was the section on the nation's need for medical care. Here the battle over health insurance, voluntary or compulsory, was entered into with zest by representatives of the medical profession, labor unions and cooperative health groups. Since the points of discussion in this group were the most controversial, the points of agreement were especially significant. All the groups represented in this section agreed that prepayment is the best way to finance medical care. All agreed that all the American people are entitled to medical care. All agreed that Federal funds must be used to finance, at any rate, some of this medical care. All agreed that the people—the consumers of medical care—have a right to establish voluntary insurance plans on a cooperative basis and that legal restrictions upon such right, now existing in a number of States, should be removed.

Despite these points of agreement, there remained a basic area of disagreement: How to prepay medical care? How to set up the insurance? The compulsory health insurance faction did not yield. But the principle of voluntary health insurance won out.

The report of the Maternal and Child Health Section contains so much of special pediatric interest that it will be reserved for more detailed review next month.

A report which has particular bearing on current thinking in the Academy is that of the subcommittee on medical personnel of the Section on Professional Personnel. It is therefore quoted in full as follows:

REPORT OF SUBCOMMITTEE ON MEDICAL PERSONNEL OF THE SECTION ON PROFESSIONAL PERSONNEL

Your Committee finds that the following major forces are creating an increased demand for physicians:

1. The increasing complexity of medical care.
2. An increasing health consciousness of the people.
3. The increasing requirements of government services for physicians.
4. The increasing number of administrative, teaching and research positions requiring physicians.

In view of this increase in demand, attention should be devoted to increasing the output of physicians in the years ahead. There are several means by which this may be accomplished. Medical educators should carefully survey existing medical schools to determine how they may best increase the number of their graduates without lowering standards. Additional medical schools are another source of supply. Six new medical schools have been organized in the past six years and the development of several others is being planned.

The Committee recognizes that more Negro physicians should be trained. It also recognizes that this problem is part of the larger problem of improving the opportunities for the education of Negroes in general, in order that there may be a larger supply of Negroes qualified to enter medical schools. The Committee recommends that effective action to improve this situation at all levels be initiated.

Your Committee calls attention to the fact that good medical education is fundamental to good

medical care and that American medical education leads the world. Efforts to increase the supply of physicians must assure the continuance of these high standards.

A continuing study of the extent to which existing medical schools are meeting the demands of the country for physicians is a responsibility of medical educators. The Committee is pleased to report that such a study is about to start under the sponsorship of the Council on Medical Education and Hospitals of the American Medical Association and the Association of American Medical Colleges. It is recommended that this study evaluate the extent to which expansion of existing schools is desirable and possible.

Intelligent planning with respect to the supply of physicians requires periodic analyses of the demand for physicians, both as to number and special qualifications. To this end studies should be developed which will furnish more precise indices for measuring the magnitude of demand.

The increasing complexity of medical education has markedly increased the cost. As a result, the problem of maintaining the present supply and quality of physicians is definitely a problem of financing.

Possible sources for additional financial support are:

1. Private contributions.
2. State and community appropriations.
3. Federal appropriations.

Your Committee recommends that increased efforts be made to secure additional contributions from the public at large as well as state and community governments. The general public does not fully appreciate their obligations to medical education in return for the benefits that they enjoy. There is evidence to indicate that local support will be insufficient to meet the financial needs of a sound and expanding program of medical education and that some form of Federal support will be necessary. Federal appropriations should entail no Federal control of the administration, curriculum and student admissions of the medical schools. Continuity of support should be assured. Funds should be granted in such a way as to increase rather than decrease the stimulus and responsibility for local support of the schools from both private and public sources.

Support will be needed in three areas: for general operation, for capital improvements, and for student support. In allocating funds for capital improvements, consideration should be given to improving the quality of medical education as well as the number of physicians trained.

With respect to student support, funds should be provided in such a way as to widen the opportunity for medical training of qualified individuals throughout the nation. Federal aid to students should carry no obligation to serve in any specified capacity after graduation.

Respectfully submitted:

RAYMOND E. ALLEN
WALTER L. BLOEDORN
DONALD G. ANDERSON
JOSEPH L. JOHNSON
DAVID D. RUTSTEIN, *Secretary*
LOWELL REED, *Chairman*

During the final morning of the Assembly, Quincy Howe gave a masterful summary of the section reports. After noting briefly the significant findings of each, he made a very timely and cogent observation:

"All these section reports call for more and more facts. Of course, none of these sections has yet got the complete story. That will never be told. Some of them are just beginning to pioneer. All of them need to correlate what they already know. But we Americans, as a people, seem to have a blind passion for facts as facts. We have an almost mystical faith in statistics. Now, the collection of facts is a necessary and rewarding enterprise, but it is not a substitute for action. It is not a substitute for something that is even more difficult than action, and that is thought. Too many of us simply collect facts simply to avoid having to do anything about it. . . .

"I am not going to tell you people what all the facts that your various sections have gathered together mean. I don't know. But I am sure a lot of you do. In some of the fields your sections have covered you will, of course, want to go out and gather more facts. Rightly! But in other cases I am sure that you have enough facts to spell out some answers; and in still other cases I bet you know the answers already and your next step is to do something about them. . . ."

PUBLIC HEALTH, NURSING AND MEDICAL SOCIAL WORK

LEONA BAUMGARTNER, M.D., *Contributing Editor*

INCIDENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES APRIL 25-MAY 22, 1948

THE accompanying table summarizes the incidence of nine important communicable diseases, based on weekly telegraphic reports from State health departments. The reports from each State for each week are published in PUBLIC HEALTH REPORTS under the section "Incidence of Disease."

NUMBER OF REPORTED CASES OF 9 COMMUNICABLE DISEASES IN THE UNITED STATES DURING THE 4-WEEK PERIOD APRIL 25–MAY 22, 1948, THE NUMBER FOR THE CORRESPONDING PERIOD IN 1947, AND THE MEDIAN NUMBER OF CASES REPORTED FOR THE CORRESPONDING PERIOD, 1943–47

Division	Current period	1947	5-year median	Current period	1947	5-year median	Current period	1947	5-year median
	Diphtheria			Influenza*			Measles		
United States	611	785	785	4,575	15,461	5,272	114,983	34,109	104,755
New England	27	52	27	19	62	62	6,720	7,818	8,089
Middle Atlantic	85	177	120	22	33	33	28,603	5,454	14,927
East North Central	104	100	117	114	277	277	28,170	6,942	19,422
West North Central	42	74	74	40	857	102	5,978	3,967	5,337
South Atlantic	124	114	142	1,736	7,254	1,399	6,924	3,771	6,866
East South Central	62	51	52	174	1,371	388	2,046	1,552	2,269
West South Central	92	96	124	2,000	4,484	2,245	11,104	2,066	3,310
Mountain	35	57	57	303	893	461	6,892	1,457	3,724
Pacific	40	64	99	167	230	230	18,546	1,082	7,313
	Meningococcus meningitis			Poliomyelitis			Scarlet fever		
United States	274	331	712	440	126	126	7,891	7,989	15,612
New England	8	20	34	0	3	5	1,056	692	2,023
Middle Atlantic	53	53	156	27	14	14	2,348	2,490	4,577
East North Central	59	73	133	23	9	9	2,388	2,303	4,013
West North Central	35	34	49	37	17	6	499	681	1,153
South Atlantic	21	50	93	67	15	16	449	503	1,276
East South Central	33	28	71	16	5	7	151	237	339
West South Central	29	35	68	191	15	26	160	142	319
Mountain	8	3	15	12	5	5	271	319	765
Pacific	28	35	93	67	43	29	569	622	888
	Smallpox			Typhoid and paratyphoid fever			Whooping cough		
United States	5	39	41	242	255	281	7,158	14,589	10,548
New England	0	0	0	15	23	20	397	842	965
Middle Atlantic	0	2	0	18	27	31	900	2,198	2,193
East North Central	0	11	16	36	58	39	891	2,588	1,683
West North Central	2	10	8	7	10	10	455	590	343
South Atlantic	0	2	2	60	31	51	1,059	2,066	1,629
East South Central	2	3	6	27	19	25	367	659	468
West South Central	1	2	4	57	49	64	1,972	3,432	1,341
Mountain	0	9	4	4	6	16	504	597	536
Pacific	0	0	2	18	32	24	613	1,617	1,617

* New York, North Carolina, and Pennsylvania excluded: New York City and Philadelphia included.

Data furnished by the Division of Public Health Methods, United States Public Health Service.

Diseases Above Median Incidence

Measles.—The number of cases of measles rose from 102,680 during the preceding 4 weeks to 114,983 during the 4 weeks ended May 22. The incidence was 3.4 times the number of cases reported for the corresponding period in 1947, which was, however, a comparatively low measles year, but it was only about 10 percent above the 1943-47 median. In the New England and East South Central sections the incidence was below the normal expectancy and in the South Atlantic section the number of cases was only slightly higher than the median for the preceding 5 years, but in the other 6 sections the increases over the median expectancy ranged from 1.1 times the median in the West North Central section to 3.4 times the median in the West South Central section.

Poliomyelitis.—The number of cases of poliomyelitis rose from 126 during the preceding 4-week period to 440 during the current 4 weeks. The incidence was 3.5 times that reported for these weeks in 1947, which number (126 cases) also represents the 1943-47 median. An increase of this disease is expected at this season of the year, but the current number of cases represents a larger increase at this time than has normally occurred in preceding years. While each section of the country except New England contributed to the relatively high incidence, the greatest excesses over the 5-year medians were reported from the West North Central and West South Central sections. Of the total cases Texas reported 179, California 62, South Carolina 46, New Jersey 16, Iowa 14, Florida 12, Alabama 11, and Illinois, South Dakota, and Louisiana 10 each; 85 percent of the reported cases occurred in those 10 states which represent every section of the country except the New England and Mountain sections. Since the beginning of the year there have been 947 cases of poliomyelitis reported as compared with 894 and 810 for the corresponding period in 1947 and 1946, respectively.

Diseases Below Median Incidence

Diphtheria.—While the incidence of diphtheria was about the same as during the preceding 4 weeks, the number of cases (611) reported during the 4 weeks ended May 22 was less than 80 percent of the 1943-47 median for the corresponding periods. In the East South Central section the incidence was about 20 percent above the seasonal expectancy and in the New England section the number reported was normal, but in all other sections the numbers of cases were considerably below the medians for the preceding 5 years. For the country as a whole the current incidence was the lowest on record for these same weeks.

Influenza.—For the current 4 weeks there were 4,575 cases of influenza reported, as compared with 15,461 for the corresponding period in 1947 and a median of 5,272 for the preceding 5 years (1943-47). The number of cases in each section was below the 1947 figure, and the numbers were below the median in all sections except the South Atlantic; in that section the number of cases was 1.2 times the 5-year median. With the exception of the year 1946 when 3,873 cases were reported for these same weeks, the current incidence was the lowest for this period since 1938 when 2,796 cases were reported.

Meningococcus meningitis.—The number of cases (274) of meningococcus meningitis reported for the 4 weeks ended May 22 was less than 85 percent of the number reported for the corresponding period in 1947 and less than 40 percent of the median for the preceding 5 years. After a period of unusually high incidence this disease has dropped to a level more nearly normal for a nonepidemic year, with each section of the country sharing in the favorable situation that now exists. The median for the preceding 5 years contains 3 years of unusually high meningitis incidence; the average incidence for this period during nonepidemic years is approximately 240 cases. A decline in this disease is normally expected at this season of the year, but the decline during the current 4-week period from the preceding 4 weeks was not as great as has occurred in preceding years.

Scarlet fever.—The number of cases of scarlet fever dropped from 8,312 during the preceding 4 weeks to 7,891 during the 4 weeks ended May 22. The number of cases was only slightly below the record low incidence of 1947, but it was 50 percent below the 1943-47 median. In each section of the country the incidence was below the 5-year median expectancy. This disease has been on a gradual decline since 1944; during that year there were approximately 26,000 cases reported during the period corresponding to the one under consideration.

Smallpox.—There were 5 cases of smallpox reported during the current 4-week period, 1 each in Missouri, Kansas, Alabama, Mississippi, and Louisiana. During the corresponding period in 1947

there were 39 cases reported and the 1943-47 median was 41 cases. The East North Central section reported none as compared with a 5-year median of 16, and the West North Central section reported 2 cases as compared with a median of 8 cases, with minor declines from the medians in other sections. For the country as a whole the current incidence was the lowest on record for this period.

Typhoid and paratyphoid fever.—The incidence of these diseases (242 cases) during the current 4 weeks was slightly below the 1947 figure for this period and was about 85 percent of the 1943-47 median. In the South Atlantic section the number of cases (60) was 1.2 times the 5-year median and in the East South Central section the incidence was about normal, but in all other sections the numbers of cases were below the normal expectancy. For the entire country the current incidence was the lowest for this period in the 20 years for which data are available in this form.

Whooping cough.—The number of cases (7,158) of whooping cough was less than 50 percent of the 1947 incidence for the corresponding 4-week period and less than 70 percent of the median for the preceding 5 years. In the West South Central section the number of cases (1,972) was 1.5 times the median expectancy and in the West North Central section the incidence (455 cases) was 1.3 times the normal incidence, but in all other sections the number of cases was lower than the seasonal expectancy.

Mortality, All Causes

For the 4 weeks ended May 22 there were 36,439 deaths from all causes reported to the National Office of Vital Statistics by 93 large cities. The median number for the preceding 3 years was 36,246 deaths. The number of deaths was higher than the median during each of the first 3 weeks of the 4-week period, but during the last week the number of deaths was 2 percent below the median for the corresponding week in the 3 preceding years.

BOOK REVIEWS

DENTAL CARIES, Bernhard Gottlieb, M.D., (University of Vienna), D.M.D. Hon. (University of Bonn), and LL.D. Hon. (Loyola University, Chicago). $10.00, 222 illustrations and 7 color plates, 262 pages. Lea and Febiger, Philadelphia, 1947.

In this volume Dr. Gottlieb elaborates his views as to the etiology, pathology, clinical aspects and prophylaxis of dental caries. In considerable measure he departs from the prevalently advocated chemo-bacterial theory of the cause of tooth decay, which places emphasis solely on the deleterious effects on the teeth of acids formed through carbohydrate fermentation. Gottlieb believes that caries is initiated through the action of proteolytic bacteria which act on the organic elements of the tooth, especially the lamellae of the enamel and the tubules of the dentin. Having breached the tooth's defenses through these channels, he believes that the interior of the tooth becomes susceptible to the decalcifying effects of acids formed through fermentation of carbohydrate residues in the oral cavity. The author gives the impression that he considers the tooth as being essentially inert in so far as physiologic changes within the tooth are concerned. Regions of increased density adjacent to carious zones he interprets as due to the re-precipitation of calcium salts which have been mobilized in the area of active decay, then redeposited in a zone where the capacity for holding the dissolved salts in solution is lessened. As a means for the prevention of caries he recommends the impregnation of the exposed surfaces of the intact teeth with a 10% solution of silver nitrate; this is to be followed immediately by the application of a saturated solution of calcium chloride. This treatment, he implies, will render the organic tissues impervious to the invasion of proteolytic organisms, and thus will seal off the enamel lamellae and the tubules against invasion by destructive micro-organisms or by acids.

Illustrations, mostly of histologic sections of teeth, are used lavishly to supplement the author's thesis. The reader is impressed by the wealth of clinical material and the thought the author has used in the preparation of this excellent work of reference. The content is not easy to master in a single reading. The effectiveness of the volume would have been enhanced if the author had devoted his first chapters to the elaboration of his hypotheses, providing clear distinction between his views and those of conflicting schools of thought, as well as between established fact and premises. In view of the incompleteness of knowledge in the field of dental disease, a reader should properly be left with the consciousness that much remains to be learned relating to the role which physiologic mechanisms exert on the tooth throughout the period of post-eruptive maturation. Instead, this text implies that the problems relating to dental caries now have been solved.

JULIAN D. BOYD

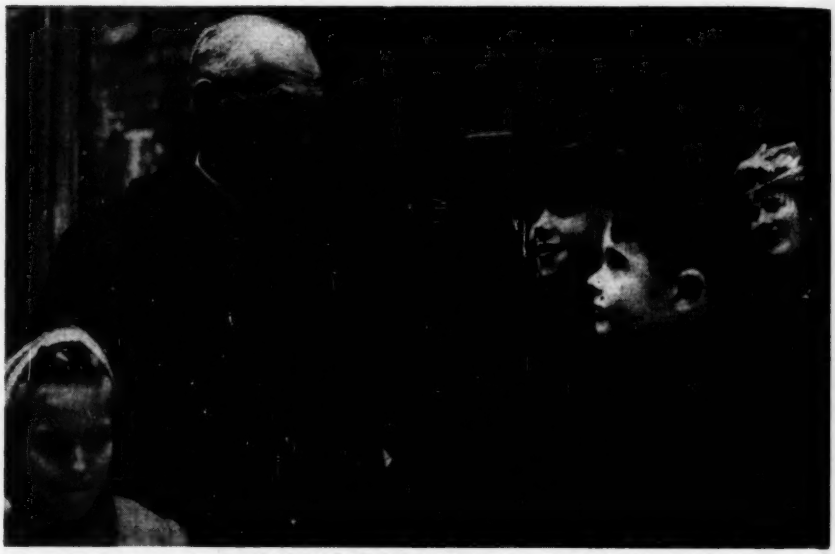
THE SCIENTIFIC PAPER—HOW TO PREPARE IT, HOW TO WRITE IT, Sam F. Trelease. $2.00, 152 pages, 8 figures. The Williams & Wilkins Co., Bailtimore, 1947.

The earlier text, published first as a mimeographed pamphlet under the title, "Preparation of Scientific and Technical Papers," has been thoroughly revised and largely rewritten. The directions given are for the preparation of a thesis or dissertation, but they apply also to the writing of other types of scientific papers, and to the preparation of manuscripts on scientific or technical subjects. The book serves as a useful guide and reference in this particular field. It is unfortunate that literature references are not given in the form of the Quarterly Cumulative Index Medicus. The style, therefore, in this respect differs considerably from that ordinarily used in medical literature.

The importance of a book of this type and its usefulness to writers in medical fields cannot be emphasized too much. Unfortunately, a great deal of material coming from clinical and research workers fails to meet its best level because its preparation is so inadequate or ill defined that the reader does not get the ideas that are in the writer's mind. Much of this is due to lack of technical knowledge of how to put a paper together. The book, therefore, can be recommended fully to anyone wishing to learn more about adequate preparation of manuscripts.

HUGH MCCULLOCH

INTERNATIONAL NEWS AND REPORTS



DR. HELMHOLZ VISITING SCHOOL CHILDREN IN THE RUSSIAN ZONE OF VIENNA. MRS. HELMHOLZ IS AT RIGHT.

Dr. Henry Helmholz, of the Mayo Clinic, Rochester, Minn., is serving as chief medical consultant in Europe for the United Nations International Children's Emergency Fund. The Fund is now helping to feed some 4,000,000 children in 12 European countries. Many of these children are in very poor physical condition. Two out of every three are T.B.-infected, so extensive findings show.

Dr. Helmholz is now working with Dr. Johannes Holm of Denmark and others on a program that calls for the testing of 50,000,000 European children in order to find the one out of three who is not yet infected with tuberculosis. These children will then be vaccinated against it with BCG vaccine. The United Nations Children's Fund is financing this unprecedented undertaking. It is one of the 25 agencies for whom help is now being sought through the campaign of the American Overseas Aid-United Nations Appeal for Children.

* * *

Dr. Thomas Parran, former chief of the U. S. Public Health Service, has joined the staff of the United Nations International Children's Emergency Fund to head a temporary mission to the Far East. He is making a study preparatory to the extension of special forms of UNICEF aid for the benefit of mothers and children there. The survey is expected to cover The Philippines, China, Hong Kong, French Indo-China, Malaya, Singapore, Indonesia, Thailand, Burma, Ceylon, India, and Pakistan.

Dr. Parran's mission is in line with policies established by the Fund's 26-nation Executive Board, which recently directed that in any future allocations special consideration be given to the needs of children in countries outside Europe—in particular those which suffered the devastation of war. Prospects of expanding these operations have been improved by increased potential contributions from the United States and other governments, and by the public's response to the appeal for aid for children on a global scale.

It is expected that the Fund's support will be given for the most part to assisting the various governments in setting up special demonstration programs in child feeding and in the control of

tuberculosis, including the organization and operation of programs for administering BCG vaccines. Support will also be given to projects for the training of child-health and child-welfare personnel.

Dr. C. K. Lakshmanan, director of the All India Institute of Hygiene and Public Health in Calcutta, will work with Dr. Parran in this effort. Dr. Lakshmanan is well known for his activities in promoting international health, having served as chairman of the Indian delegation to the International Health Conference in New York in 1946, at which Dr. Parran presided.

NEWS AND ANNOUNCEMENTS

Dr. John McK. Mitchell has been appointed Dean of the University of Pennsylvania Medical School. For the past two years Dr. Mitchell has conducted the survey of pediatric education in all accredited U. S. medical schools in the Academy's Study of Child Health Services.

* * *

Dr. John Aikman, assistant professor of pediatrics, University of Rochester School of Medicine and Dentistry, Rochester, N.Y., has been awarded the 1948 Albert David Kaiser Medal for outstanding medical service. Dr. Aikman, who has been in practice in Rochester for more than 30 years, received the award at a meeting of the Rochester Academy of Medicine, May 4. He is a past chairman of the AMA Section on Pediatrics.

* * *

Deaths: Two Academy fellows have died recently: Dr. Albert M. Wise of Brooklyn, N.Y., died April 3; and Dr. Samuel McC. Hamill of Philadelphia, Pa., died May 3.

EDITORIAL

THE following statement was received in the form of a "letter to the Editor' from Dr. Edna Miller of New York City, who commented, "What better way is there to reach pediatricians than through the medium of their new publication PEDIATRICS?":

"Dentists are constantly informing parents and others in charge of young children as to the need for an early 'first visit with the dentist.'

"Much of the irremedial damage, dentally and psychologically, is due to the pain and traumatic experience that necessarily follow the discovery of decayed teeth by the dentists, or the uncomfortable sensation of an acute dental abscess felt by a child.

"When children are first seen by the dentists at the age of two and one-half or three years, and thereafter at frequent, regular intervals, the procedures are usually painless; or, if pain is unavoidable, the dentist has already impressed the child with his sincerity. He is then no longer a stranger, visited only at a moment of emergency, who does unfamiliar, unpleasant things with elaborate equipment. Instead, he is the child's friend, using customary technics and commonplace instruments. Pedodontists find few children among their regular, 'old' patients who are uncooperative, or who present any behavior problem during treatment.

"Dental societies, school authorities, and lay organizations work continually to provide parents of young children with health information and guidance. Yet there remain many who appear for dental care for the first time at the age of five or six years, in pain, and in need of extractions.

"The pediatrician is the one person who can help to bridge the gap in our application of health knowledge. He sees the child regularly from earliest infancy. His advice and suggestions are welcomed by parents. Yet he may not refer a young child for dental examination unless the defects are glaring.

"Today, when the dentist has adequate technics at his disposal for diagnosis, prevention and treatment of oral diseases, defects and abnormalities, the pediatrician can grant his patients an inestimable service, in the fields of dental and mental health, merely by early routine referral to children's dentists?"

(signed) Edna Miller, D.M.D., M.P.H.

The principal theme of the letter emphasizes the emotional control of children who come under pediatric dental care, and the advantages that come from close cooperation among doctors, dentists and parents. But Dr. Miller's comment is timely and important also because it calls attention to one of the most frequent problems in child health; and because this frequency makes it so commonplace that it is considered no problem at all. The statement also serves to focus attention on: what is dental caries; how can it be prevented; and through what agencies can care be provided? Is dental care, alone, adequate to prevent caries? Suppose every child went to the dentist regularly for cleaning and whatever the dentist does for a child's teeth, would the problem of caries be solved?

Many dentists believe still that caries is a matter of carbohydrate metabolism and the presence of certain bacteria in the mouth.*

The control of dental caries is far more than such care alone. Underlying it all is a

* Gottlieb, B., Dental Caries, Lea and Febiger, Philadelphia, 1947. (See review on page 141.)

state of nutrition of the child, and the work of Boyd, Tisdall, Johnston, their co-workers and many others, suggests that this basic nutrition may be more important than local dental service. Good nutrition then becomes an integral part of a program of prevention. Shall the dentist become a nutritionist, or shall the problem be handled by a combination of services from different groups?

Also, how far can our increasing understanding of growth and development with its varied and complex factors be used in the control of dental caries? Does cultivation of good mouth and chewing habits of infants and young children enter in the incidence of caries later? Do emotional strain, physical fatigue, and infection play a part, even indirectly? Do enlarged and infected tonsils and adenoids bear any relation to dental caries, mouth deformity and defective eating and breathing habits? Are infected tonsils and carious teeth joint results of a common cause? How far does prenatal and maternal nutrition go in the prevalence of caries and its control?

Dental caries is a condition that is so common and widespread that it may be accepted as a natural result of growth in children. It was listed as one of the major physical defects found in draftees inducted into military service in the recent war. A former Surgeon General of the United States Public Health Service has declared recently that it is the main challenge at the present in the arrangements proposed for rendering Federal aid to children through funds set aside for school health services.

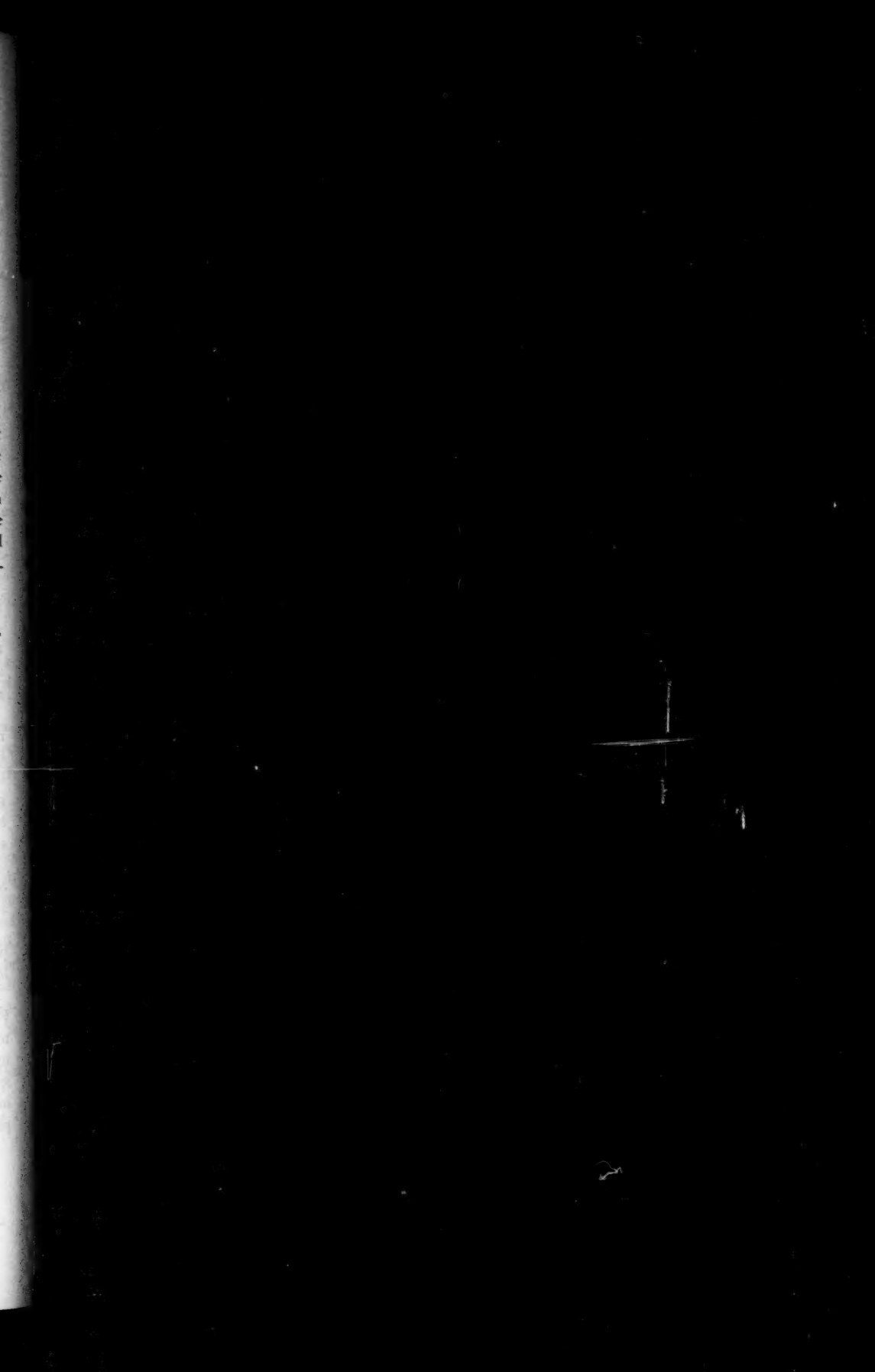
What are the criteria of dental caries and when does caries constitute a physical defect? The U. S. Public Health Service has set up certain quantitive criteria which are in general use. But these seem entirely arbitrary and artificial. From the standpoint of child health, even one carious area in a child's tooth may indicate a trend towards more serious lesions later; and, if early recognition can lead to prevention, such insignificant lesions, which fall short of U.S.P.H.S. standards for defects, become of great importance.

The relatively recent discovery that the chemical element fluorine enters in the nutrition of teeth may recast a great many proposals for caries control. Much remains to be learned about the influence of fluorine and especially methods for using it. Its use may resolve itself into some such practice as that for iodine in areas where endemic goiter is prevalent. Shall the dentist apply fluorine to children's teeth, shall the child be given daily tablets containing fluorine, or should fluorine be added to municipal sources of drinking water? These are methods to be considered and decided on. Other chemicals and elements also may enter into the problem. Recent work on disturbances of bone metabolism suggest, for example, that protein enters into the picture, and teeth are also bone structure.

How shall these questions be worked out and through what means shall the information be made available to the public to promote child health? Close reading of pediatric literature reveals little that is being done for the solution of these problems.

The American Society for Dentistry for Children and the American Academy of Pedodontics have an interest in this matter, as well as the American Academy of Pediatrics. Other dental and pediatric societies are concerned, though those mentioned seem to be the logical ones to approach the problem. These organizations, each in their own sphere, have recently shown an aroused interest in specialized, professional education in this field. Already several institutions are setting up combined teaching units comprised of nutritionists, pediatricians, dentists, and others to work out an educational

program. It would seem that the main job is to coordinate resources already available, in a plan to use the knowledge to be applied. The House of Representatives in the present Congress has voted and sent to the Senate a bill which provides for the appropriation to the Federal Security Agency of, among other things, one million dollars for a national campaign to train dentists in the use of sodium fluoride to check dental decay. The Study of Child Health Services, completed recently by the American Academy of Pediatrics, included a survey of facilities for dental care and this received the support of the American Dental Association. A secondary phase of the Study included a survey of facilities for professional education. Information derived from this source is in a form never before available. It should serve to point a way of approach.

Education of the public as well as professional education, seems equally important. Sound, healthy teeth are part of sound, healthy bodies. Sound, healthy bodies are acquired by the individual's own desire to secure them. The desire can be introduced and inculcated by training, but its attainment rests with the individual. Health cannot be bought. It must be sought after and cultivated through education and training. The Study of Child Health Services indicates very clearly that most of the children are under health and medical care of general practitioners, and that trained specialists, both pediatricians, and probably pediatric dentists, see and care for only small fractions of the total number of children. Therefore, Dr. Miller's letter is sound in so far as this small group of children is concerned. But the same principle must apply also to all children.

HUGH MCCULLOCH